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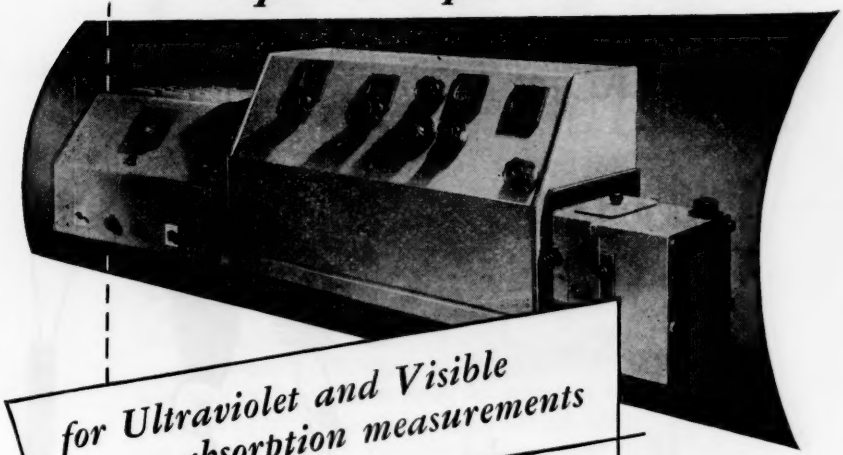

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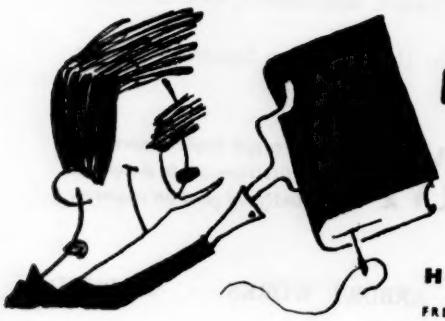

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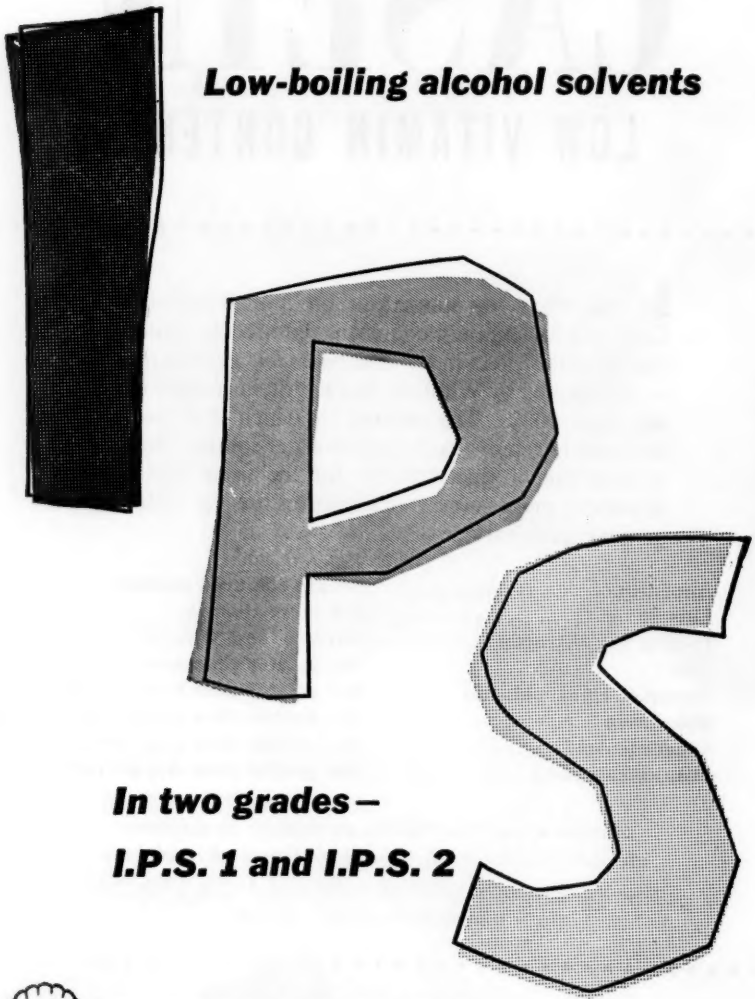

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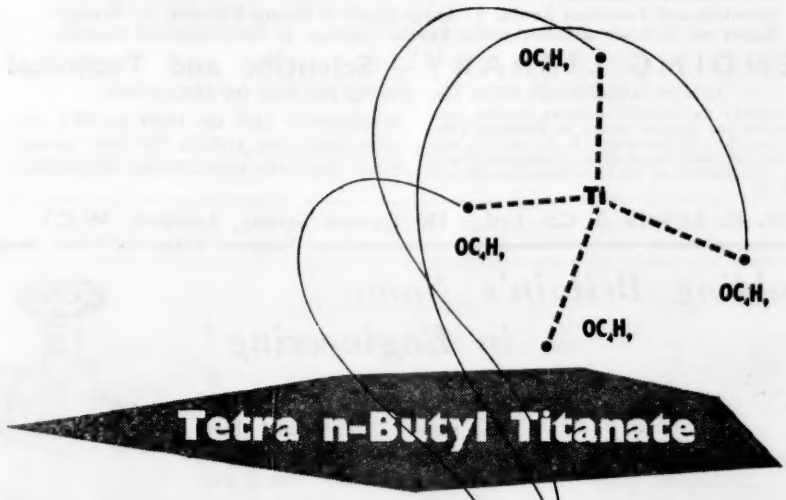

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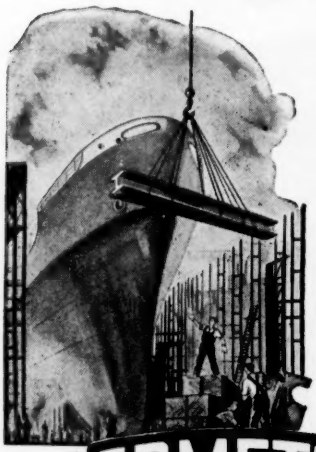

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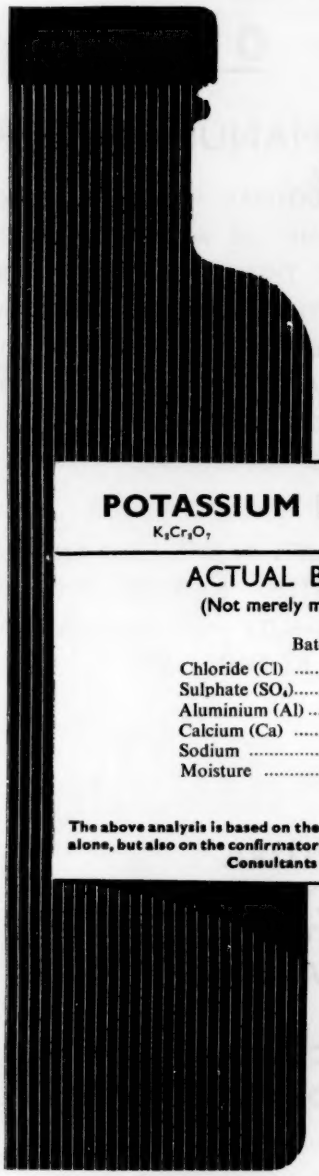

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(Not merely maximum impurity values)

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Chloride (Cl)	0·0005%
Sulphate (SO_4)	0·002%
Aluminium (Al)	0·00013%
Calcium (Ca)	0·0024%
Sodium	no reaction
Moisture	0·022%

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The Stereospecificity of Carbanion Reduction Processes.

By D. H. R. Barton and C. H. Robinson.

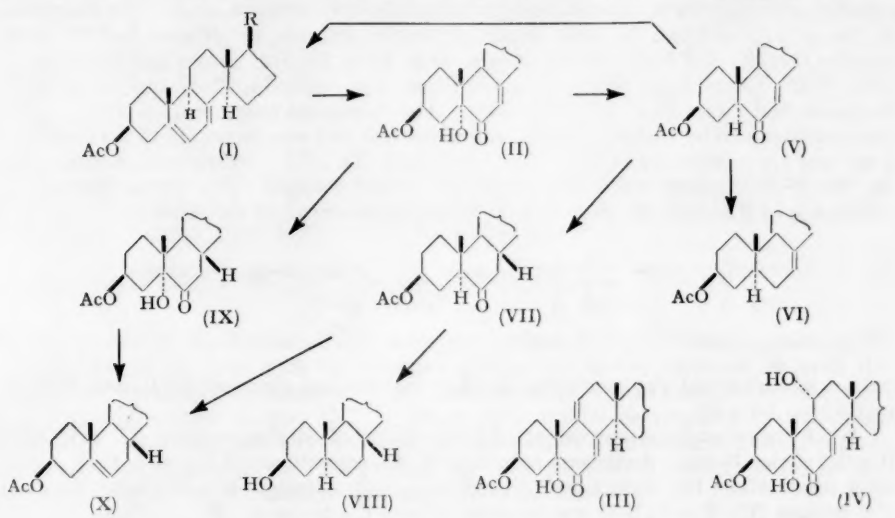
[Reprint Order No. 5326.]

Various transformations based upon 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one are described, including the reduction of this compound and of the derived 3β-acetoxyergosta-7 : 22-dien-6-one by lithium and liquid ammonia to afford products with the β-configuration at $C_{(8)}$. As a result of these and numerous related observations it is concluded that such reductions usually afford the thermodynamically more stable products. This conclusion is, however, only part of a broader generalisation that carbanion reduction processes in alkaline media which involve the creation of asymmetric centres usually appear to afford the stereochemically more stable products. A possible explanation for this is suggested.

A convenient route for the conversion of ergosterol into brassicasterol is reported.

The original objective of the investigations outlined in this paper was the introduction of oxygenated functions at $C_{(11)}$ in derivatives of ergosterol. However, certain theoretical conclusions were drawn from the work and these eventually dictated additional experimentation on the stereospecificity of carbanion reduction processes.

Oxidation of ergosterol acetate (I; R = C_9H_{17}) with chromic acid gave 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one (II; R = C_9H_{17}) (Burawoy, *J.*, 1937, 409), hydrogenated to the 22 : 23-dihydro-derivative (II; R = C_9H_{19}). It was originally intended to extend the conjugated system of (II; R = C_9H_{17}) to that of (III; R = C_9H_{17}); vinylogous β-addition of hydroxyl ion (or its equivalent) to this would afford compounds such as the dihydroxy-ketone (IV; R = C_9H_{17}). The oxidising action of bromine was first studied. Treatment of the ergosta-7 : 22-dien-6-one (II; R = C_9H_{17}) with bromine gave a dibromide. Since the ergost-7-en-6-one (II; R = C_9H_{19}) was inert under the same brominating conditions, this compound must be the side-chain dibromide (II; R = $C_9H_{17}Br_2$). At this

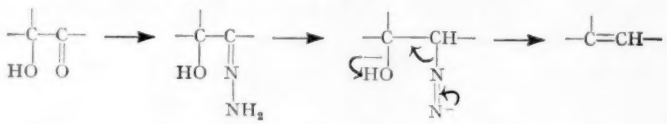


stage in the investigation Professor C. W. Shoppee (Swansea) very kindly informed us of his interest in the same objective and we therefore concentrated on other aspects of the chemistry of 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one (II; R = C_9H_{17}).

Reduction of the hydroxyketone (II; R = C_9H_{17}) with zinc dust and acetic acid removed the hydroxyl group. Catalytic hydrogenation of the product (V; R = C_9H_{17}) over platinum gave ergost-8(14)-enyl acetate, but hydrogenation over palladised calcium carbonate furnished 3β-acetoxyergost-7-en-6-one (V; R = C_9H_{19}). Wolff–Kishner reduction of (V; R = C_9H_{17}), followed by reacetylation, gave 5-dihydroergosteryl acetate (VI; R = C_9H_{17}). The infra-red spectrum of the ketone (V; R = C_9H_{17}) showed bands at 1675 and 1620 (αβ-unsaturated ketone), at 1733 and 1234 (acetate), and at 966 cm.$^{-1}$ (*trans*-22 : 23-ethylenic linkage), in agreement with the assigned constitution.

Reduction of the ketone (V; R = C_9H_{17}) with lithium and liquid ammonia (Wilds and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 5360, 5366), followed by reacetylation, gave 3β-acetoxyergost-22-en-6-one (VII; R = C_9H_{17}). The steric course of the reduction was established by Wolff–Kishner reduction of the product to ergost-22-en-3β-ol (VIII; R = C_9H_{17}) (Barton, Cox, and Holness, *J.*, 1949, 1771). Similar lithium and liquid ammonia reduction of the ergost-7-en-6-one (V; R = C_9H_{19}), followed by reactylation, gave 3β-acetoxyergostan-6-one (VII; R = C_9H_{19}), affording ergostan-3β-ol (VIII; R = C_9H_{19}) on Wolff–Kishner reduction. 3β-Acetoxyergostan-6-one was also available by hydrogenation of (VII; R = C_9H_{17}). The configurations at $C_{(5)}$ in the ketones (VII; R = C_9H_{17} and R = C_9H_{19}), and hence in (V; R = C_9H_{17} and R = C_9H_{19}), are confirmed by molecular-rotation considerations. Thus the observed $[M]_D$'s for (VII; R = C_9H_{17} and R = C_9H_{19}) are −191° and −82° respectively. The calculated values, based on the known molecular rotation of ergost-22-ene (Barton, Cox, and Holness, *loc. cit.*) and computed from the standard tables of Barton and Klyne (*Chem. and Ind.*, 1948, 755), are −182° and −86° respectively.

Reduction of the hydroxy-ketone (II; R = C_9H_{17}) with lithium and liquid ammonia, followed by reacetylation, afforded 3β-acetoxy-5α-hydroxyergost-22-en-6-one (IX; R = C_9H_{17}). Catalytic hydrogenation gave the dihydro-derivative (IX; R = C_9H_{19}), also available by the lithium–ammonia route from the hydroxyergostanone (II; R = C_9H_{19}). Wolff–Kishner reduction of the dihydro-derivatives (IX; R = C_9H_{17} and R = C_9H_{19}) afforded, after reacetylation, 3β-acetoxyergosta-5 : 22-diene (brassicasteryl acetate) (X; R = C_9H_{17}) and 3β-acetoxyergost-5-ene (X; R = C_9H_{19}) respectively. The brassicasteryl acetate was further characterised as the derived sterol and its benzoate. The process reported here represents a convenient partial synthesis of brassicasterol. The conversion of (IX) into (X) is based the observations by Barton, Holness, and Klyne (*J.*, 1949, 2456; see also Ruzicka and Meldahl, *Helv. Chim. Acta*, 1940, **23**, 513; Ames and Bowman, *J.*, 1951, 2752; Leonard and Sentz, *J. Amer. Chem. Soc.*, 1952, **74**, 1704) and especially by Heymann and Fieser (*ibid.*, 1951, **73**, 5252). The theoretical interpretation of this type of reaction advanced by Barton, Holness, and Klyne (*loc. cit.*) was derived from the findings of Jeger and his collaborators (*Helv. Chim. Acta*, 1951, **34**, 1577; and references there cited) on the Wolff–Kishner reduction of αβ-unsaturated ketones. The mechanism of the conversion of (IX) into (X) may be more simply represented by the scheme:



Such a scheme would also encompass satisfactorily the case discussed by Barton, Holness, and Klyne (*loc. cit.*).

When cholestan-6-one was subjected to the Bamford–Stevens reaction (*J.*, 1952, 4735) it gave cholest-5-ene. Analogous reduction of the ergostenone (VII; R = C_9H_{17}) gave, after recetylation, the ergostadiene (X; R = C_9H_{17}), although in poor yield. Likewise, the dienone (V; R = C_9H_{17}) was reconverted into the triene (I; R = C_9H_{17}).

From the theoretical point of view the formation of the thermodynamically more stable 8β-derivatives from unsaturated ketones of the types (II) and (V) is worthy of more extended comment. In Table 1 we have collected examples of the reduction of αβ-unsaturated ketones with lithium and liquid ammonia reported in the literature. To this

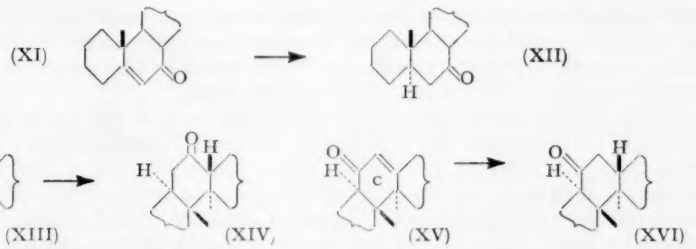
list we have added the reduction of cholest-5-en-7-one (XI) to cholestan-7-one (XII). Also, in the triterpenoid field, we have found that reduction of 12-oxo-β-amyr-9(11)-en-3β-yl acetate (XIII) gives, after reacetylation, 12-oxo-β-amyran-3β-yl acetate (XIV) and

TABLE 1.

System reduced	No. of examples	Confign. of product	Most stable confign.	Refs.
Steroid				
4-en-3-one	5	5α	5α	1, 2
5-en-7-one	1	5α	5α	3
7-en-6-one	4	8β	8β	3
8-en-7-one	1	8β, 9α	8β, 9α	4
8-en-11-one	4	8β, 9α	8β, 9α	5, 6, 7, 8
8(14)-en-15-one	3	8β, 14α	8β, 14α	9
Triterpenoid				
8-en-7-one (lanosterol series)	1	8β, 9α	8β, 9α	10
9(11)-en-12-one	1	9α	9α	3
12-en-11-one	1	13β	13β	3

1, Barton, Ives, and Thomas, *Chem. and Ind.*, 1953, 1180; *J.*, 1954, 903. 2, W. S. Johnson, Bannister, Bloom, Kemp, Pappo, Rogier, and Szmuszkovicz, *J. Amer. Chem. Soc.*, 1953, **75**, 2275. 3, This paper. 4, Alt and Barton, *J.*, 1954, 1356. 5, Sondheimer, Yashin, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1952, **74**, 2696; Sondheimer, Mancera, Rosenkranz, and Djerassi, *ibid.*, 1953, **75**, 1282. 6, Schoenewaldt, Turnbull, Chamberlin, Rheinhold, Erickson, Ruyle, Chemerda, and Tishler, *ibid.*, 1952, **74**, 2696. 7, Heusler, Heusser, and Anliker, *Helv. Chim. Acta*, 1953, **36**, 652. 8, Burke, Turnbull, and Wilson, *J.*, 1953, 3237; Bladon, Henbest, Jones, Lovell, and Woods, *J.*, 1954, 125. 9, Barnes, Barton, and Laws, *Chem. and Ind.*, 1953, 616; Barton and Laws, *J.*, 1954, 52. 10, Barton and Thomas, *Chem. and Ind.*, 1953, 172; *J.*, 1953, 1842.

that 11-oxo-β-amyr-12-en-3β-yl benzoate (XV) analogously affords 11-oxo-β-amyran-3β-yl acetate (XVI). In every case so far studied the configuration of the reduction product is the more stable one.*



The reduction of αβ-unsaturated ketones by dissolving metals in liquid ammonia can be conveniently represented by the following scheme (cf. Burton and Ingold, *J.*, 1929, 2022; Birch, *Quart. Reviews*, 1950, **4**, 69; Wilds and Nelson, *loc. cit.*):

(XVII)

The formulation of the dianion (XVII) as an intermediate does not, of course, exclude the co-ordination of Li^+ ions with the negative charges to furnish ion-pairs, or even the formation of covalent C–Li bonds (cf. Wilds and Nelson, *loc. cit.*) so long as these dissociate in a reversible manner to give (XVII), which may usually be regarded as the entity protonated. The reduction may, therefore, be classified as a carbanion reduction process and the stereochemistry of the final product (at the β-position) is thus governed by the stereochemistry of the protonation of the carbanion (XVII).

* This conclusion was also advanced, on the basis of more limited evidence, by Dr. L. H. Sarett (Merck and Co.) in a lecture at the University of New Brunswick, Canada, in August, 1953. The point was further illustrated by a stereospecific reduction of an αβ-unsaturated ester (see Sarett, Arth, Lukes, Beyler, Poos, Johns, and Constantin, *J. Amer. Chem. Soc.*, 1952, **74**, 4974; Arth, Poos, Lukes, Robinson, Johns, Feurer, and Sarett, *ibid.*, 1954, **76**, 1715).

It is of interest that the stereochemical course of the reduction of conjugated dienes and trienes (in the steroid series) (see Table 2) by dissolving metals is also always such as to afford the thermodynamically more stable product. This is likewise true for the analogous

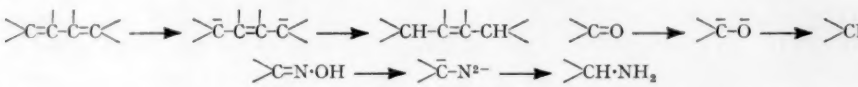
TABLE 2.

System reduced	No. of examples	Products	Confign. of products	Most stable confign.*	Refs.
5 : 7-diene (10-normal) ...	2	7-ene	5α	5α	1, 2, 3, 4
5 : 7-diene (10-*iso*)	1	7-ene	5α	5α	5, 6, 7
6 : 8-diene	1	7-ene	9α	9α	8, 9
5 : 7 : 9(11)-triene	1	7-ene	5α, 9α	5α, 9α	10
		5 : 7-diene	9α	9α	
		7 : 9(11)-diene	5α	5α	
5 : 7 : 14-triene	1	6 : 8(14)-diene	5α	5α	11

* Based on the corresponding saturated structure of normal (*trans-anti-trans*) stereochemistry except as otherwise specified.

1, Windaus and Brunken, *Annalen*, 1928, **460**, 225. 2, von Reichel, *Z. physiol. Chem.*, 1934, **226**, 146. 3, Windaus and Langer, *Annalen*, 1934, **508**, 105. 4, Schenck, Buckholz, and Wiese, *Ber.*, 1936, **69**, 2696. 5, Windaus, Dithmar, and Fernholz, *Annalen*, 1932, **493**, 259. 6, Heilbron, Moffet, and Spring, *J.*, 1937, 411. 7, Cole, *J.*, 1952, 4969. 8, Windaus, Linsert, and Eckhardt, *Annalen*, 1938, **534**, 22. 9, Barton and Cox, *J.*, 1949, 214. 10, Bergmann and Klacsmann, *J. Org. Chem.*, 1948, **13**, 21. 11, Barton and Brunn, *J.*, 1951, 2728.

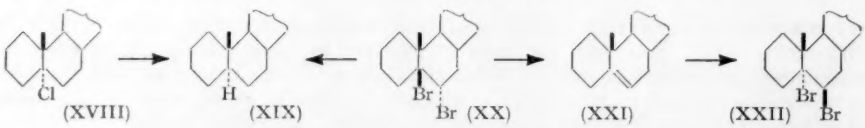
reductions of ketones to secondary alcohols and of oximes to amines (see Barton, *Experientia*, 1950, **6**, **316**; *J.*, 1953, 1027; and references there cited). These three procedures can all be represented as carbanion reduction processes (cf. Birch, *loc. cit.*):



One may conclude, in general, that reduction of multiple bond systems through intermediate carbanions usually affords the thermodynamically more stable products. A spectacular example of this synthetically useful principle has been given recently by W. S. Johnson *et al.* (*J. Amer. Chem. Soc.*, 1953, **75**, 2275).

It appears that the stereochemical preferences discussed in this paper are most simply rationalised if the carbanion has a preferred tetrahedral configuration. This would be separated from the inverted tetrahedral arrangement by only a low energy barrier (cf. ammonia and tertiary amines) in order to explain the ready racemisation of saturated carbanions (see, for example, Gilman's "Organic Chemistry," Vol. I, p. 383, John Wiley and Sons Inc., New York, 1943). If this is true, the unshared electron pair might be expected to occupy an orbital approximating in size to a C–H bond. Thus the preferred configuration would be that which, on protonation, would afford the more stable arrangement of the asymmetric centre.

In support of these ideas we have found that reduction of 5-chlorocholestane (XVIII) (for configuration see Bernal, Crowfoot, and Fankuchen, *Trans. Roy. Soc.*, 1940, *A*, **239**, 135; Crowfoot in "Vitamins and Hormones," Vol. II, p. 409, Academic Press, New York,



(XVIII) (XIX) (XX) (XXI) (XXII)

1944) with lithium and liquid ammonia affords an almost quantitative yield of cholestane (XIX). Cholestane was also the only saturated product from the reduction of 5-chlorocholestane with sodium and alcohol. Likewise in agreement, the reduction of 5 : 6α-dibromocoprostane (XX) (see Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 1066) by lithium and liquid ammonia gave, along with the (not unexpected) cholest-5-ene (XXI), cholestane as sole saturated product. Similar reduction of the stereoisomeric diaxial

5 : 6β-dibromocholestane (XXII) gave only cholest-5-ene : this is not unexpected from the stereochemical point of view (cf. Barton, *loc. cit.*). Professor C. W. Shoppee (Swansea) has kindly informed us that both 3α- and 3β-bromocholestane afford cholestane-3β-carboxylic acid on carboxylation of their derived Grignard reagent. This important observation is of obvious relevance to the discussion in the present paper.

Dr. Hans Heusser of the Eidg. Technische Höchschule (Zürich) has kindly told us that he has also observed the reduction of 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one by lithium and liquid ammonia to a 8β-compound. We thank Dr. Heusser cordially for this information.

Experimental

For general experimental detail see *J.*, 1952, 2339. $[\alpha]_D$ were measured in $CHCl_3$, ultraviolet absorption spectra in EtOH. Infra-red spectra were kindly determined by Messrs. Glaxo Laboratories Ltd. in carbon disulphide solution.

3β-Acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one (II; R = C_9H_{17}) *and -7-en-6-one* (II; R = C_9H_{19}).—The following modification of Burawoy's method (*loc. cit.*) was found to be suitable. To a suspension of ergosteryl acetate (20 g.) in " AnalaR " acetic acid (400 ml.) was added with vigorous stirring chromium trioxide (13·6 g.) in 80% acetic acid (80 ml.) at room temperature. The mixture, after being stirred for a further hour, was left overnight, then, after addition of methanol (3 ml.), diluted with water. The precipitated solid was digested with ethyl acetate (250 ml.) on the steam-bath. Cooling and filtration gave the desired acetoxy-ketone (4·4 g., 20%), m. p. 258—262° (decomp.). Crystallisation from ethyl acetate gave the pure material as plates, m. p. 263—265° (decomp.), $[\alpha]_D$ −5° (*c*, 1·00), $\lambda_{max.}$ 250 mμ (ε 14,000).

Catalytic hydrogenation for 2 hr. in 9 : 1 dioxan–acetic acid with a platinum catalyst gave *3β-acetoxy-5α-hydroxyergost-7-en-6-one*, m. p. (from ethyl acetate) 252—255° (decomp.), $[\alpha]_D$ +12° (*c*, 1·07), $\lambda_{max.}$ 248 mμ (ε 14,000) (Found : C, 76·05; H, 10·1. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·25%).

3β-Acetoxyergosta-7 : 22-dien-6-one (V; R = C_9H_{17}).—3β-Acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one (2 g.) in " AnalaR " acetic acid (150 ml.) was refluxed for 1 hr. with portionwise addition of zinc dust (15 g.). Chromatography of the product over alumina and elution with 4 : 1 light petroleum (b. p. 40—60°)–benzene gave *3β-acetoxyergosta-7 : 22-dien-6-one*, m. p. (needles from methanol) 184—186°, $[\alpha]_D$ −17° (*c*, 1·49), −16° (*c*, 1·02), $\lambda_{max.}$ 245 mμ (ε 16,000) (Found : C, 79·2; H, 10·05. $C_{30}H_{46}O_3$ requires C, 79·25; H, 10·2%). Hydrogenation of this acetoxy-ketone in acetic acid overnight with a platinum catalyst afforded ergost-8(14)-en-3β-yl acetate, identified by m. p. mixed m. p. and rotation {$[\alpha]_D$ ±0° (*c*, 1·59)}.

Hydrogenation in ethyl acetate for 5 hr. with palladised calcium carbonate gave *3β-acetoxyergost-7-en-6-one* (V; R = C_9H_{19}), m. p. (needles from methanol) 153—155°, $[\alpha]_D$ +5° (*c* 0·63), $\lambda_{max.}$ 245 mμ (ε 14,000) (Found : C, 79·2; H, 10·35. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). Wolff–Kishner reduction of this ketone (100 mg.) under the normal conditions followed by re-acetylation and chromatography gave 3β-acetoxyergosta-7 : 22-diene (m. p. and mixed m. p.).

Bromination of 3β-Acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one.—The ketone (500 mg.) in 1 : 1 chloroform–acetic acid (50 ml.) containing anhydrous sodium acetate (880 mg.) was treated with bromine (190 mg.) in " AnalaR " acetic acid (20 ml.) at room temperature for 30 min. Crystallisation of the product from benzene–light petroleum (b. p. 40—60°) afforded *3β-acetoxy-5α-hydroxy-22 : 23-dibromoergost-7-en-6-one* as needles, m. p. 213—215° (decomp.), $[\alpha]_D$ +9° (*c*, 1·08) (Found : C, 57·0; H, 7·6; Br, 25·2. $C_{30}H_{46}O_4Br_2$ requires C, 57·15; H, 7·35; Br, 25·35%). Attempted bromination of 3β-acetoxy-5α-hydroxyergost-7-en-6-one under the same conditions gave back starting material (m. p. and mixed m. p.).

3β-Acetoxyergost-22-en-6-one (VII; R = C_7H_{17}).—3β-Acetoxyergosta-7 : 22-dien-6-one (780 mg.) in dry ether (50 ml.) was added with stirring to a solution of lithium (700 mg.) in liquid ammonia (250 ml.). Excess of lithium was destroyed by the addition of ammonium chloride, and the mixture worked up in the usual way. Reacetylation, chromatography over alumina, and elution with light petroleum (b. p. 40—60°) furnished *3β-acetoxyergost-22-en-6-one*, m. p. (plates from chloroform–methanol) 162—164°, $[\alpha]_D$ −42° (*c*, 1·18) (Found : C, 78·95; H, 10·35. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%).

Wolff–Kishner reduction of this ketone (100 mg.) in the usual way and crystallisation of the product from methanol gave ergost-22-en-3β-ol (VIII), m. p. 154—156°, $[\alpha]_D$ −11° (*c*, 1·53), undepressed in m. p. on admixture with an authentic specimen (Barton, Cox, and Holness, *J.*, 1949, 1771).

3β-*Acetoxyergostan*-6-*one* (VII; R = C_9H_{19}).—3β-Acetoxyergost-7-en-6-one was subjected to lithium and liquid ammonia reduction under the same conditions to give, after reacetylation, chromatography over alumina, and elution with light petroleum (b. p. 40—60°), 3β-*acetoxyergostan*-6-*one*, m. p. (plates from chloroform–methanol) 142—144°, $[\alpha]_D$ −18° (*c*, 1·23) (Found: C, 79·25, 78·55; H, 10·9, 10·4. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). This ketone was also obtained (m. p. and mixed m. p.) by catalytic hydrogenation of 3β-acetoxyergost-22-en-6-one in ethyl acetate with a palladised calcium carbonate catalyst. Wolff–Kishner reduction gave ergostan-3β-ol, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +13° (*c*, 1·09)}.

3β-*Acetoxy*-5α-*hydroxyergost*-22-*en*-6-*one* (IX; R = C_9H_{17}).—3β-Acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one (1·0 g.; dried at 100° for 8 hr.) in suspension in dry ether (200 ml.) was added rapidly to a solution of lithium (300 mg.) in liquid ammonia (200 ml.) with vigorous stirring. The excess of lithium was immediately destroyed with solid ammonium chloride. Reacetylation of the product and crystallisation from ethyl acetate–methanol afforded 3β-*acetoxy*-5α-*hydroxyergost*-22-*en*-6-*one* (500 mg.), m. p. 249—253°, $[\alpha]_D$ −74° (*c*, 0·66) (Found: C, 75·95; H, 10·05. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·25%).

3β-*Acetoxy*-5α-*hydroxyergostan*-6-*one* (IX; R = C_9H_{19}).—(*a*) 3β-Acetoxy-5α-hydroxyergost-7-en-6-one (300 mg.; dried at 100° for 8 hr.) in suspension in dry ether (60 ml.) was added rapidly with vigorous stirring to a solution of lithium (100 mg.) in liquid ammonia (50 ml.). Working up as in the preceding case afforded 3β-*acetoxy*-5α-*hydroxyergostan*-6-*one* (140 mg.), m. p. 252—256°, $[\alpha]_D$ −53° (*c*, 2·00) (Found: C, 75·5; H, 10·4. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%).

(*b*) 3β-Acetoxy-5α-hydroxyergost-22-en-6-one (200 mg.) was hydrogenated in ethyl acetate with palladised calcium carbonate (at 60° owing to the sparing solubility of the unsaturated ketone). Crystallisation of the product from ethyl acetate–methanol afforded 3β-acetoxy-5α-hydroxyergostan-6-one, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ −57° (*c*, 1·19)}.

Wolff–Kishner Reduction of 3β-*Acetoxy*-5α-*hydroxyergost*-22-*en*-6-*one*.—The ketone (300 mg.) and hydrazine hydrate (2 ml.; 100%) in ethanol (2 ml.) were heated in a sealed tube at 180° for 2 hr. Sodium (300 mg.) in ethanol (4 ml.) was then added and heating continued overnight. The products from two such reactions were reacetylated (400 mg.) and chromatographed over alumina. Elution with light petroleum (b. p. 40—60°) afforded 3β-acetoxyergosta-5 : 22-diene (brassicasteryl acetate) (180 mg.) as plates (from chloroform–methanol), m. p. 158—159°, $[\alpha]_D$ −64° (*c*, 1·70), −63° (*c*, 1·00). Hydrolysis with methanolic potassium hydroxide gave ergosta-5 : 22-dien-3β-ol, m. p. (from chloroform–methanol) 150—151°, $[\alpha]_D$ −60° (*c*, 1·28). Benzoyl chloride–pyridine furnished the benzoate, m. p. (from chloroform–methanol) 169—172°, $[\alpha]_D$ −36° (*c*, 1·00). For the corresponding derivatives of brassicasterol Windaus and Welsch (*Ber.*, 1909, **42**, 612) reported m. p. 157—159°, m. p. 148°, $[\alpha]_D$ −64°, and m. p. 167°, respectively.

Wolff–Kishner Reduction of 3β-*Acetoxy*-5α-*hydroxyergostan*-6-*one*.—The ketone (330 mg.) was reduced as above. Re-acetylation of the product, chromatography over alumina, and elution with light petroleum afforded 3β-acetoxyergost-5-ene (X; R = C_9H_{19}) (200 mg.), m. p. (from chloroform–methanol) 152—154°, $[\alpha]_D$ −52° (*c*, 1·42), −50° (*c*, 1·08). The derived sterol had m. p. 146—148°, $[\alpha]_D$ −45° (*c*, 1·65). Fernholz and Ruigh (*J. Amer. Chem. Soc.*, 1940, **62**, 3346) recorded for these substances m. p. 145°, $[\alpha]_D$ −46°, and m. p. 158°, $[\alpha]_D$ −46°, respectively.

Alkaline Decomposition of Some Steroid Toluene-p-*sulphonylhydrazones*.—Cholestan-6-one (386 mg.), prepared from cholest-5-ene according to the directions of Windaus (*Ber.*, 1920, **53**, 488), and toluene-*p*-sulphonhydrazide (Freudenberg and Blümmel, *Annalen*, 1924, **440**, 51) (186 mg.) in hot ethanol (5 ml.) containing one drop of concentrated hydrochloric acid were heated under reflux for 20 min. The solvent was removed *in vacuo* and the residue, in dioxan (5 ml.) and ethylene glycol (5 ml.; redistilled) containing sodium (150 mg.), was refluxed for 45 min. Crystallisation of the product from chloroform–methanol gave cholest-5-ene (60 mg.), identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ −49° (*c*, 1·43)}.

3β-Acetoxyergosta-7 : 22-dien-6-one (228 mg.) (see above), subjected to the same reaction gave, after chromatography of the re-acetylated product over alumina, ergosteryl acetate (74 mg.), identified by m. p., mixed m. p., and absorption spectrum.

3β-Acetoxyergost-22-en-6-one (120 mg.) (see above) treated in the same way afforded, after chromatography of the re-acetylated product over alumina, 3β-acetoxyergosta-5 : 22-diene (40 mg.) identified by m. p., mixed m. p. (see above), and rotation {$[\alpha]_D$ −63° (*c*, 0·70)}.

Reduction of Some αβ-*Unsaturated Ketones with Lithium and Liquid Ammonia*.—Cholest-5-ene was converted into cholest-5-en-7-one, m. p. 128—129°, $[\alpha]_D$ −127° (*c*, 1·71), $\lambda_{max.}$ 238 mμ (ε 11,000) by the method used by Fieser *et al.* (*J. Amer. Chem. Soc.*, 1949, **71**, 2226) for the oxidation of cholesteryl acetate.

The unsaturated ketone (200 mg.) in dry ether (25 ml.) was added with vigorous stirring to a solution of lithium (60 mg.) in liquid ammonia (40 ml.). Excess of lithium was destroyed by acetone. Chromatography of the product over alumina and elution with light petroleum gave cholestan-7-one (145 mg.), m. p. (plates from chloroform–methanol) 114—115°, $[\alpha]_D$ −42° (*c*, 1·09), undepressed in m. p. on admixture with an authentic specimen (see Barton and Rosenfelder, *J.*, 1951, 1048).

12-Oxo-β-amyr-9(11)-en-3β-yl acetate (150 mg.) was reduced in the same way and the reacetylated product chromatographed over alumina. Elution with 4 : 1 light petroleum (b. p. 40—60°)–benzene gave 12-oxo-β-amyran-3β-yl acetate (80 mg.), m. p. (from chloroform–methanol) 291—293°, undepressed in m. p. on admixture with an authentic specimen (prepared from β-amyrin acetate according to Spring's directions, *J.*, 1933, 1345).

11-Oxo-β-amyr-12-en-3β-yl benzoate (300 mg.) was reduced in the same way and the product (after hydrolysis with 10% potassium hydroxide in 1 : 1 methanol–dioxan under reflux for 3 hr. and then acetylation) chromatographed over alumina. Elution with 1 : 1 benzene–light petroleum (b. p. 40—60°) gave 11-oxo-β-amyran-3β-yl acetate, m. p. (plates from chloroform–methanol) 330—332° (evacuated capillary), $[\alpha]_D$ +6° (*c*, 1·07). Ruzicka and Jeger (*Helv. Chim. Acta*, 1945, **28**, 209) recorded m. p. 341° (corr.), $[\alpha]_D$ +7°, for this compound.

Reduction of 5-Chlorocholestane.—(*a*) The chloro-compound (300 mg.) in dry ether (30 ml.) was added to a solution of lithium (150 mg.) in liquid ammonia (40 ml.) with stirring. Crystallisation of the product (negative Beilstein test) from chloroform–methanol gave cholestane (18 mg.), m. p. and mixed m. p. 79—80°, $[\alpha]_D$ +24° (*c*, 1·22).

(*b*) The chloro-compound (150 mg.) in *n*-propanol (10 ml.) was heated under reflux with addition of sodium (150 mg.) for 15 min. The product (125 mg.; negative Beilstein test) gave a positive tetranitromethane test due to the presence of cholest-4- and -5-ene (cf. Mauthner, *Monatsh.*, 1907, **28**, 1113; Wettstein *et al.*, *Helv. Chim. Acta*, 1946, **29**, 627). A portion of the product (62 mg.) was treated with ethereal perphthalic acid at 0° for 24 hr. (uptake equiv. to 65% of olefin) and the resulting oil in chloroform (5 ml.) was treated with dry hydrogen chloride at room temperature for 20 min. Chromatography over alumina and elution with light petroleum (b. p. 40—60°) afforded cholestane (18 mg.), identified by m. p. and mixed m. p.

Reduction of the 5 : 6-Dibromocholestanes.—(*a*) 5 : 6β-Dibromocholestane (see Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 1066) (300 mg.) was reduced as described above, but with twice the quantity of lithium. Crystallisation of the total product {195 mg., 93%; negative Beilstein test; $[\alpha]_D$ −49° (*c*, 1·64)} from chloroform–methanol gave cholest-5-ene, m. p. and mixed m. p. 90—91°, $[\alpha]_D$ −50° (*c*, 1·47).

(*b*) 5 : 6α-Dibromocoprostane (see Barton and Miller, *loc. cit.*) (200 mg.) was reduced as under (*a*). The total product (129 mg., 92%) gave a negative Beilstein test and had $[\alpha]_D$ −25° (*c*, 1·67). The material (114 mg.) was treated with ethereal perphthalic acid at 0° for 63 hr. The product in chloroform (5 ml.) was treated with dry hydrogen chloride at room temperature for 20 min. and the resulting oil (94 mg.) was chromatographed over alumina. Elution with light petroleum (b. p. 40—60°) afforded cholestane (27 mg.; tetranitromethane test negative), m. p. (from chloroform–methanol) 79—80°, undepressed on admixture with an authentic specimen. The perphthalic acid uptake corresponded to 69% of cholest-5-ene. The observed rotation ($[\alpha]_D$ −25°; see above) for the total product would correspond to 62% of cholest-5-ene and 38% of cholestane.

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Syntheses in the Morphine Series. Part VI. The Synthesis of Morphine.†*

By Dov Elad and David Ginsburg.

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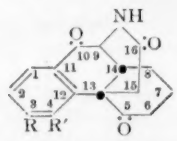
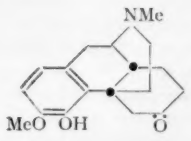
In continuation of previous experiments (Part V *) synthetic intermediates have been converted into (−)-dihydrothebainone. This constitutes a synthesis of morphine.

In Part IV of this series (Ginsburg and Pappo, *J.*, 1953, 1524) the synthesis of the tetracyclic lactam (I*a*) was described. In Part V * methods were investigated for the oxygenation at $C_{(6)}$, so that it would be possible to convert the methoxylated analogue (I*b*) into a compound such as dihydrothebainone (II). In this communication, the synthesis of the methoxylated analogue (I*b*) is described and its conversion into dihydrothebainone is reported.

(I*a*): R = R′ = H
(I*b*): R = OMe, R′ = OH

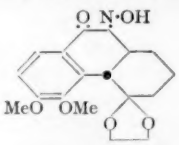


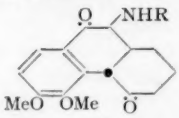


(II)

The 4-ethylene glycol ketal (III) of 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydro-10-hydroxyimino-5 : 6-dimethoxy-4 : 9-dioxophenanthrene was reduced catalytically with palladised carbon in the presence of hydrochloric acid, to give the hydrochloride of the corresponding 10-amino-compound (IV*a*) (cf. Ginsburg and Pappo, *loc. cit.*), the ketal grouping being lost during the reduction. The amine hydrochloride was suspended in chloroform containing pyridine, and the mixture was treated with acetylglycollyl chloride the 10-acetoxyacetamido-derivative (IV*b*) was obtained in high yield.

(III)





(IV*a*): R = H
(IV*b*): R = CO·CH_2·OAc

In analogy with the unique cyclisation observed with the unmethoxylated analogue of (IV*b*), which yielded the lactam (I*a*) (Ginsburg and Pappo, *J.*, 1953, 1524), treatment of (IV*b*) with toluene-*p*-sulphonic acid in the presence of ethylene glycol yielded two substances, m. p. 244—246° and 196° respectively. The higher melting product proved to be the 10-ethylene glycol ketal of the lactam (I*b*).‡ It was noted that demethylation of the 4-methoxyl group occurred during cyclisation. Thus, in the tetracyclic lactam series, demethylation of this group occurs as readily as the analogous demethylation in the tetracyclic amine series (cf. Grewe, Mondon, and Nolte, *Annalen*, 1949, **564**, 161).

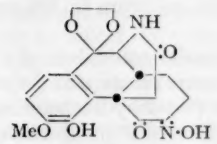
The structural assignment for the major cyclisation product, m. p. 244—246°, was made on the basis of the analytical results and the infra-red absorption spectrum which clearly showed at 5·84 μ the presence of the alicyclic carbonyl group. Although it was difficult to determine unequivocally from the infra-red spectrum whether absorption by the carbonyl group conjugated to the aromatic nucleus was absent, since the lactam function absorbs very nearly in the same region, the typical bands for the ketal grouping were present.

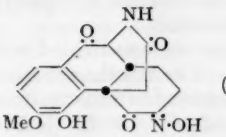
* Part V, *J.*, 1953, 2664.

† A preliminary communication on this subject has been published (Elad and Ginsburg, *J. Amer. Chem. Soc.*, 1954, **76**, 312).

‡ The numbering used for the tetracyclic products which have the skeletal structure of morphine is that used for morphine itself.

The subsequent step in the reaction sequence permitted a test of this structural assignment. The hydroxyimino-compound (V) was obtained in about 80% yield and its properties were in accord with its formulated structure. The next step afforded further convincing evidence, as careful acid treatment of (V) selectively removed the blocking group at $C_{(10)}$ without effecting hydrolysis of the oxime group at $C_{(6)}$, and the 6-hydroxyimino-5 : 10-dioxo-lactam (VI) was obtained.

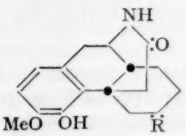
(V) 

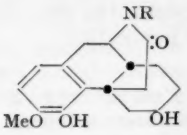


(VI)

Now that the carbonyl group at $C_{(5)}$ had served its purpose of introducing a potential oxygen function at $C_{(6)}$ (as is required, for example, in dihydrothebainone), it became necessary to remove the oxygen functions at $C_{(5)}$ and $C_{(10)}$. A serious difficulty appeared to prevent this, namely, the presence of the α-diketone system at $C_{(5)}$ and $C_{(6)}$. The alkaline conditions required in the Wolff–Kishner reduction would be expected to be sufficiently stringent to effect a benzilic acid rearrangement in ring C from its present form to a hydroxy-*cyclo*pentanecarboxylic acid system. For this reason the oxime grouping in (VI) was not hydrolysed before the reduction. Furthermore, since cases are known in which heating of a hydrazone, even in the absence of alkali, resulted in conversion of a carbonyl group into a methylene group (cf. Todd, "Organic Reactions," Vol. 4, p. 384, Wiley, New York, 1948), the Huang-Minlon procedure was used but alkali was omitted in this instance. When the temperature of the reaction mixture containing the dihydrazone of (VI) reached 140°, evolution of nitrogen began and the reduction was essentially complete in 3 hours. After isolation of the product (VII*a*), no carbonyl absorption appeared in its infra-red absorption spectrum. The 6-oxime grouping, however, remained intact. Acid hydrolysis of (VII*a*) afforded the ketone (VII*b*).

(VII*a*) : R = :N·OH
(VII*b*) : R = :O





(VIII*a*) : R = H
(VIII*b*) : R = Me

Attempted ketalisation in order to block the 6-oxo-group failed. The ketone (VII*b*) was therefore subjected directly to reduction with lithium aluminium hydride. The resulting epimeric mixture de-*N*-methyldihydrothebainols (VIII*a*) was methylated by means of formaldehyde–formic acid to yield dihydrothebainol (VIII*b*) which failed to crystallise, and apparently consisted of a mixture of the axial and equatorial racemates. Since oxidation of this mixture should give only one ketone and because of the small amount of material at hand, the isolation of the dihydrothebainols epimeric at $C_{(6)}$ was not attempted.

The behaviour of both known dihydrothebainols on oxidation by potassium *tert.*-butoxide–benzophenone was next investigated. "Dihydrothebainol A," m. p. 142°, has been prepared by electrolytic reduction or sodium amalgam reduction of (−)-dihydrothebainone (Speyer and Siebert, *Ber.*, 1921, **54**, 1519). "Dihydrothebainol B," m. p. 165°, was obtained by reduction of the ketone with a platinum catalyst in the presence of acid (Skita, Nord, Reichert, and Stukart, *ibid.*, p. 1560). Attempted stereospecific reduction of (−)-dihydrothebainone by means of sodium borohydride and lithium aluminium hydride severally was successful only in part. In both instances, mixtures of the axial and the equatorial isomer were formed. Since after repeated crystallisation the "A" isomer (probably equatorial) was obtained pure in the sodium borohydride reduction, whilst the "B" isomer (probably axial) was thus obtained from the lithium aluminium hydride reduction, it appears that each predominates in one of these reductions. However, chromatography of the mother-

liquors clearly showed that both isomers were present in each case. Although it has been shown for other alcohols in the morphine series, that the axial alcohol is oxidised much faster than its equatorial isomer, by means of potassium *tert.*-butoxide–benzophenone (Rapoport, Naumann, Bissell, and Bonner *J. Org. Chem.*, 1950, **15**, 1103), no appreciable difference in rate could be detected in the rates of oxidation of the dihydrothebainols A and B.

The semisolid racemic dihydrothebainol mixture obtained in this investigation was oxidised by means of potassium *tert.*-butoxide in the presence of benzophenone, and the racemic ketone obtained was identical in its infra-red spectrum (in the range 2—15 μ) with (−)-dihydrothebainone.

The racemic ketone was treated with one-half molar equivalent of (+)-tartaric acid in acetone solution. The salt thus obtained had the same rotation as (−)-dihydrothebainone (+)-tartrate. Conversion into the free base gave (−)-dihydrothebainone, $[\alpha]_D^{21}$ −75° (in EtOH). Values of $[\alpha]_D^{20}$ −80·12° (in EtOH) and $[\alpha]_D^{18}$ −72·5° (in absolute EtOH) have been reported (Skita *et al.*, *loc. cit.*; Schöpf and Winterhalder, *Annalen*, 1927, **452**, 232).

The synthesis of optically active dihydrothebainone constitutes the second total synthesis of morphine. Gates and Tschudi (*J. Amer. Chem. Soc.*, 1952, **74**, 1109) have accomplished the first total synthesis of morphine and their brilliant work involved the conversion of dihydrothebainone into morphine. Conditions for the cyclisation of dihydrothebainone into 1-bromodihydrocodeinone have been reported by Schöpf and Pfeifer (*Annalen*, 1930, **483**, 157). Demethylation of codeine to morphine has been reported by Rapoport, Lovell, and Tolbert (*J. Amer. Chem. Soc.*, 1951, **73**, 5900).

Rapoport has recently concluded his elegant series of proofs regarding the stereochemistry at the various asymmetric centres of the morphine molecule (Rapoport and Lavigne, *ibid.*, 1953, **75**, 5329 and references listed therein). He has shown that the B and the C ring of morphine are *cis*-locked. In both the Gates and Tschudi synthesis of morphine and in ours (cf. Ginsburg and Pappo, *J.*, 1953, 1524) compounds in which the respective rings are *trans*-locked were converted into derivatives of the natural *cis*-series. In our case, the cyclisation of the *trans*-compound to one of *cis*-configuration proceeds by an unknown mechanism. It is now clear, however, from the results of *X*-ray investigations of the morphine structure, carried out in two laboratories, that a *cis*-B : C junction exists in morphine. We are indebted to Mrs. Dorothy Hodgkin, F.R.S., for disclosing this information to us, before its publication.

Experimental

4-Ethylene Glycol Ketal of 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-10-*hydroxyimino*-5 : 6-*dimethoxy*-4 : 9-*dioxophenanthrene*.—Sodium (1·2 g.) was dissolved in dry ethanol (25 ml.) and a solution of the 4-ethylene glycol ketal of 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydro-5 : 6-dimethoxy-4 : 9-dioxophenanthrene (15·1 g.) in dry dioxan (60 ml.) was added in one portion. *n*-Amyl nitrite (11 ml.) was added and the mixture was kept in the refrigerator for 48 hr. Ether and dilute acetic acid were added with cooling. The aqueous phase was extracted with three portions of ether and the combined ether extracts were extracted with three portions of Claisen's alkali. Acidification with acetic acid precipitated the 10-hydroxyimino-derivative (12·6 g., 76%). The product obtained by this modified procedure is identical with that reported by Ginsburg and Pappo (*J.*, 1953, 1524).

10-*Amino*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-5 : 6-*dimethoxy*-4 : 9-*dioxophenanthrene Hydrochloride*.—The above hydroxyimino-compound (12·6 g.; employed without further purification) was suspended in ethanol (300 ml.) and hydrogenated in the presence of palladised charcoal (10%; 2 g.) and hydrochloric acid (35%; 6 ml.) at an initial hydrogen pressure of 60 lb./sq. in. Hydrogen uptake ceased after 2 hr. The catalyst was filtered off and the solvent removed at the water pump. Ethanol (100—150 ml.) was added to dissolve the hydrochloride, and ether was then added until the solution was turbid. After standing in the refrigerator the *amine hydrochloride* (5·5—6·5 g., 50—60%) was obtained as colourless crystals, m. p. 206—208° (decomp.). Recrystallisation from ethanol–ether raised the m. p. to 210—212° (decomp.) (Found: C, 58·0; H, 6·2; N, 4·2; Cl, 10·85. $C_{16}H_{20}O_4NCl$ requires C, 58·15; H, 6·15; N, 4·3; Cl, 10·8%).

10-*Acetoxyacetamido*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-5 : 6-*dimethoxy*-4 : 9-*dioxophenanthrene*.—The amine hydrochloride (4·5 g.) was suspended in chloroform (60 ml.), and dry pyridine (5 ml.) was added. The mixture was boiled for 2 min., then cooled in ice, and a solution of

acetylglycollyl chloride (4·4 g.) in chloroform (20 ml.) was added dropwise during 1 hr. Finally, the mixture was refluxed for 30 min. The clear light orange solution was washed twice with dilute hydrochloric acid and with water. The chloroform was removed at the water-pump, and the residual heavy oil crystallised upon trituration with ethanol. The *acetoxyacetamide* formed colourless crystals, m. p. 169—171° (from ethanol) (4 g., 76%) (Found: C, 61·7; H, 5·8; N, 3·6. $C_{20}H_{23}O_7N$ requires C, 61·7; H, 6·0; N, 3·6%). A second crop (0·5 g.) of slightly lower-melting material was obtained from the mother-liquor.

Cyclisation.—A mixture of the acetoxyacetamide (5·4 g.), ethylene glycol (30 ml.), toluene (50 ml.), benzene (30 ml.) and toluene-*p*-sulphonic acid (0·1 g.) was refluxed for 8—9 hr., with an "azeotropic" receiver to collect the volatile products. After cooling, solid sodium carbonate was added to give a slightly alkaline reaction and the two layers were separated. The ethylene glycol layer was diluted with water, the organic layer was separated, and the solvents were removed under reduced pressure. The solid residue was extracted with boiling heptane–benzene. Upon cooling, the extract deposited crystals, m. p. 193—195°. Recrystallisation raised the m. p. to 196° (from heptane–benzene). This substance was obtained in very low yield and was not further characterised.

The fraction insoluble in heptane–benzene was dissolved in boiling ethanol. After standing, the *ketal-lactam* (10-dioxalan of I*b*) crystallised, and had m. p. 244—246° (from ethanol or toluene) (Found: C, 63·2; H, 5·7; N, 4·0%; active H, 1·7. $C_{19}H_{21}O_6N$ requires C, 63·5; H, 5·9; N, 3·9%; active H, 2·0). The *mono*-2 : 4-*dinitrophenylhydrazone*, prepared in the usual way, had m. p. 241—242° (from ethanol–chloroform) (Found: N, 13·8. $C_{25}H_{21}O_8N_5$ requires N, 14·1%); the ketal group had been hydrolysed.

The Dioxo-lactam (I*b*).—The ketal-lactam (1 g.) was added to a mixture of ethanol (25 ml.) and water (10 ml.), and concentrated hydrochloric acid (5 drops) was added. The mixture was heated at 60° for 2 hr. On cooling, colourless crystals of the *dioxo-lactam* (0·5 g.), m. p. 216—218° (from heptane–benzene), were obtained (Found: C, 65·0; H, 5·5. $C_{17}H_{17}O_5N$ requires C, 64·8; H, 5·4%). The product becomes yellow in air. The 2 : 4-dinitrophenylhydrazone, prepared in the usual way, had m. p. 241—242° (from ethanol–chloroform). Admixture with the 2 : 4-dinitrophenylhydrazone reported above caused no m. p. depression.

6-*Hydroxyimino-lactam* 10-*Ketal* (V).—To a solution of sodium ethoxide [prepared from 207 mg. of sodium (0·009 mole) and 10 ml. of ethanol] were added finely powdered ketal-lactam, m. p. 244—246° (1·077 g., 0·003 mole), and dry dioxan (10 ml.). *n*-Amyl nitrite (0·41 ml.) was added with ice-cooling. After 1·5 hr. the solid material had dissolved and the solution became dark brown. The mixture was refrigerated for 24 hr. Ether (50 ml.), water (25 ml.), and acetic acid (1·5 ml.) were added and the aqueous phase was extracted with 4 additional portions of ether; the 6-*hydroxyimino*-derivative precipitated from the ether solution (650—700 mg.) had m. p. 259—260° (decomp.). The analytical sample was obtained by treatment of the highly insoluble light yellow product with boiling ethanol. The m. p. was thus raised to 265—266° (decomp.) (Found: C, 58·6; H, 5·2; N, 7·1. $C_{19}H_{20}O_7N_2$ requires 58·8; H, 5·2; N, 7·2%). Evaporation of the mother-liquor under reduced pressure yielded an additional 50 mg. of the product. The product gives a green colour with alcoholic ferric chloride.

6-*Hydroxyimino*-10-*oxo-lactam* (VI).—The 6-hydroxyimino-lactam 10-ketal (V) (1·2 g.) was refluxed in ethanol (120 ml.), water (10 ml.), and concentrated hydrochloric acid (2 ml.) for 1 hr. The solvents were removed under reduced pressure and the residue heated at 100° in a high vacuum to remove ethylene glycol. The residue weighed 1 g. The analytical sample was obtained by trituration with methanol. The pure 6-*hydroxyimino*-10-*oxo-lactam* had m. p. 212—214° (decomp.) (from methanol) (Found: C, 59·3; H, 4·5; N, 7·9. $C_{17}H_{16}O_6N_2$ requires C, 59·3; H, 4·7; N, 8·1%). The crude product was sufficiently pure to be employed in the next reaction without crystallisation.

Reduction.—The crude 6-hydroxyimino-10-oxo-lactam (VI) (1 g.) and hydrazine hydrate (1 ml.) in diethylene glycol (25 ml.) were heated on a steam-bath for 8 hr. The temperature was then raised to 165° and maintained thereat for 2 hr., nitrogen being evolved continually. After dilution with water the mixture was continuously extracted with ether for 24 hr. After removal of the ether, the oxime-lactam (VII*a*) was obtained as a very viscous oil (427 mg.). A small portion was dissolved in benzene and chromatographed over Merck's acid-washed alumina; the pure compound, micro-m. p. 210—213° (from pentane), was obtained. The substance gave a large m. p. depression on admixture with the 6-hydroxyimino-10-oxo-lactam.

Mixture of Racemic Dihydrothebainols.—(*a*) The oxime-lactam (VII*a*) (400 mg.) was refluxed in ethanol (50 ml.), water (5 ml.), and hydrochloric acid (3 ml.) for 5 hr. The solvents were removed under reduced pressure, the residue was treated with chloroform, the chloroform solu-

tion was washed with water, and the solvent again removed under reduced pressure. It was not possible to prepare a ketal of the residual ketone.

(*b*) To a solution of lithium aluminium hydride (2 g.) in tetrahydrofuran (70 ml.) was added a solution of the free ketone (from *a*) (300 mg.) in tetrahydrofuran (30 ml.). The mixture was refluxed for 120 hr. under nitrogen. The solvent was removed under reduced pressure and the residue was treated with dilute hydochloric acid. Continuous extraction (24 hr.) with ether removed acid-insoluble material. The aqueous phase was evaporated to dryness under reduced pressure and the amine hydrochloride was extracted several times with boiling acetone. The acetone solution contained the hydrochloride of de-*N*-methyldihydrothebainol.

(*c*) The acetone was removed under reduced pressure, the semi-solid residue was treated with aqueous ammonia, and the free amine extracted with chloroform. After removal of the solvent, methylation was carried out by formaldehyde–formic acid as described for the unmethoxylated analogue (cf. Ginsburg and Pappo, *J.*, 1953, 1536). After the usual working-up a mixture of racemic dihydrothebainols was obtained as a sticky solid.

Dihydrothebainol A.—To a solution of dihydrothebainone ($[\alpha]_D^{21}$ −75°; 2 g.) in methanol (25 ml.) was added finely powdered sodium borohydride (700 mg.) at room temperature. The temperature rose to 40°. The mixture was set aside for 2 hr. The solvent was evaporated under reduced pressure; dilute hydrochloric acid was added to the residue, and the acid solution was treated with excess of concentrated aqueous ammonia. The product was extracted with 6 portions of ether. Evaporation of the ether gave a solid residue (2 g.). Many recrystallisations from ethyl acetate or aqueous ethanol gave dihydrothebainol A (280 mg.), m. p. 140—142° (after some softening at 135°). When heated in a drying pistol the material softens. Speyer and Siebert (*loc. cit.*) report m. p. 142° (with sintering at 138°) for dihydrothebainol A.

Dihydrothebainol B.—A solution of dihydrothebainone ($[\alpha]_D^{21}$ −75°; 3 g.) in tetrahydrofuran (50 ml.) was added during 10 min. to a solution of lithium aluminium hydride (3 g.) in tetrahydrofuran (100 ml.), and the mixture was refluxed for 6 hr. The solvent was removed under reduced pressure and dilute ammonia solution was added to the residue carefully with cooling. Continuous ether-extraction (48 hr.) of the alkaline mixture followed by evaporation of the ether gave a solid (2·8 g.). Recrystallisation from ethyl acetate gave dihydrothebainol B (300 mg.), m. p. 166—169°. Skita *et al.* (*loc. cit.*) report m. p. 165° for this compound.

Optically Active Dihydrothebainone.—Dihydrothebainol A or B (200 mg.) and benzophenone (1·2 g.) were added to a mixture of dry potassium *tert.*-butoxide (prepared from 100 mg. of potassium and 15 ml. of *tert.*-butanol) in dry benzene (20 ml.), and the mixture was refluxed for 3 hr. After cooling, hydrochloric acid (3N; 15 ml.) was added and the acid layer was separated. The benzene solution was extracted with hydrochloric acid (3N; 2 × 15 ml.), and the combined acid extracts were washed with benzene and with ether. The acid solution was basified with concentrated ammonia solution and the product was extracted with chloroform. The yield of dihydrothebainone isolated from dihydrothebainol A was 96 mg. and that from dihydrothebainol B was 105 mg. The infra-red spectra of 10 mg. samples of each crude product in chloroform showed that no more alcohol was present and that the concentration of ketone in each case was practically identical.

Racemic Dihydrothebainone.—Oxidation of the crude racemic dihydrothebainols (110 mg.) as above yielded the racemic ketone (48 mg.). The infra-red spectrum of this product was identical in the range 2—15 with that of optically active dihydrothebainone.

Resolution of Synthetic Dihydrothebainone.—To racemic dihydrothebainone (42 mg.) in acetone (10 ml.) was added (+)-tartaric acid (10 mg.) in acetone (10 ml.). The acetone solution was treated with charcoal, filtered, and concentrated to about one-half of its original volume. The (+)-tartrate of (−)-dihydrothebainone was deposited and was filtered off {28 mg.; m. p. 110°, $[\alpha]_D^{20\cdot5}$ +18·2° (*c* 1·1 in H_2O)}. The analytical sample was dried in a high vacuum for 24 hr. (Found: C, 58·2; H, 6·2. Calc. for $C_{22}H_{29}O_9N$: C, 58·5; H, 6·5%). The (+)-tartrate of authentic (−)-dihydrothebainone (from natural sources) had $[\alpha]_D^{20\cdot5}$ +18·1° (*c* 1·1 in H_2O).

To this tartrate (25 mg.) in water (5 ml.) was added concentrated ammonia solution (2 ml.), and the mixture was extracted with chloroform. The extract was washed several times with water, and the solvent was evaporated. The residue of (−)-dihydrothebainone (synthetic) was allowed to crystallise. Filtration afforded (−)-dihydrothebainone (12 mg.), m. p. 122—151°, $[\alpha]_D^{21}$ −75° (*c*, 0·77 in EtOH).

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N-*Methylthiamine.*

By P. Nesbitt and P. Sykes.

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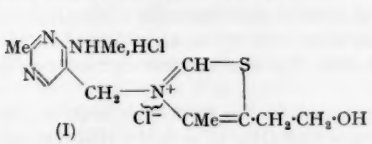
N-Methylthiamine [5-2′-hydroxyethyl-4-methyl-3-(2-methyl-4-methylamino-5-pyrimidyl)methylthiazolium chloride hydrochloride], required as a thiamine analogue, has been prepared in good yield. The effect, on the reactions of a substituted 5-pyrimidylmethyl group, of replacing an amino- by a methylamino-group in the adjacent 4-position is investigated and discussed.

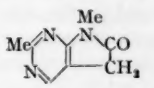
After a study (Sykes and Todd, *J.*, 1951, 534) of the mechanism of the oxidation of thiamine (vitamin B_1) by one-electron oxidising agents and the disproportionation of thiamine disulphide in hot high-boiling hydroxylic solvents, a model compound having certain features was required. Essentially it must be a 5-pyrimidylmethylthiazolium compound containing a modified amino-group in the 4-position of the pyrimidine nucleus that would be unable to undergo a dehydrative ring-closure with the *N*-formyl group liberated by the action of alkali on the thiazole nucleus. *N*-Methylthiamine [5-2′-hydroxyethyl-4-methyl-3-(2-methyl-4-methylamino-5-pyrimidyl)methylthiazolium chloride hydrochloride] (I) was thought to be suitable.

N-Methylthiamine is mentioned in the literature (Schultz, *Z. physiol. Chem.*, 1940, **265**, 113) only in reference to its biological testing, no indication being given of the method of preparation. A potential intermediate in its preparation, 5-aminomethyl-2-methyl-4-methylaminopyrimidine (II; R = NH_2), is mentioned in U.S.P. 2,377,395, being prepared from ethyl 4-chloro-2-methyl-5-pyrimidylacetate (V; R′ = Cl, R″ = CO_2Et) (Cerecedo and Pickel, *J. Amer. Chem. Soc.*, 1937, **59**, 1714) *via* 2-methyl-4-methylamino-5-pyrimidylacetic acid (II; R = CO_2H) and the corresponding ethyl ester and amide; the desired amine (II; R = NH_2) was obtained by Hofmann degradation of the amide. We were, however, unable to repeat this series of reactions outlined: treatment of the chloro-compound (V; R′ = Cl, R″ = CO_2Et) with ethanolic methylamine, followed by hydrolysis of the methylamide (II; R = CO·NHMe), led to the expected acid (II; R = CO_2H), but the subsequent reactions followed a different course. Attempted esterification of this acid yielded, not the expected ethyl ester (II; R = CO_2Et), but the lactam (III). In attempts to convert this lactam into the desired amide (II; R = CO·NH_2), it was recovered unchanged on treatment with ethanolic or liquid ammonia, and it was reconverted into the

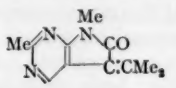


(I)

(II)



(III)



(IV)

acid (II; R = CO_2H) by aqueous ammonia or alkali. On attempting to recrystallise the compound from acetone it was converted into an *iso*propylidene derivative (IV), the reaction being facilitated by the presence of a little dry ammonia; this behaviour, which is not duplicated by the formally similar, *N*-methyl-α-(2-methyl-4-methylamino-5-pyrimidyl)-acetamide (II; R = CO·NHMe), is somewhat surprising but is reminiscent of oxindole which also forms an *iso*propylidene derivative (Wahl and Livovschi, *Bull. Soc. chim.*, 1938, **5**, 653), though with somewhat greater difficulty. No carbonyl condensation compound derived from the more closely analogous *N*-methyloxindole has been recorded.

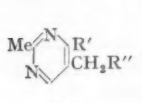
A crude, unstable methyl ester (II; R = CO_2Me) was prepared by means of diazomethane but with ammonia again led to the lactam (III). Nor could the desired amide be obtained by the action of ammonia on the methylamide (II; R = CO·NHMe). Attention was therefore turned to the hydrazide (II; R = CO·NH·NH_2), which was prepared from the methyl ester, lactam, and methylamide.

The hydrazide was treated with nitrous acid by Cerecedo and Pickel's method (*loc. cit.*), and with amyl nitrite by the method of Todd *et al.* (*J.*, 1936, 1601). The former gave the

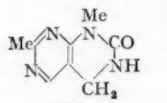
tetra-azanaphthalene derivative (VI) [by cyclisation of the *iso*cyanate (II; R = NCO)] and the latter gave largely the lactam (III) arising because the azide (II; R = CON_3) acts as an acylating agent, under the various conditions employed, on the adjacent methylamino-group. That the methods are satisfactory for hydrazides having an amino-group in the 4-position of the pyrimidine nucleus was demonstrated by the preparation of 4-amino-2-methyl-5-pyrimidylacethydrazide (V; R′ = NH_2, R″ = CO·NH·NH_2) by the action of hydrazine on the corresponding amide, and its conversion into 4-amino-2-methyl-5-ethoxy-(and methoxy)carbonylaminomethylpyrimidine (V; R′ = NH_2, R″ = NH·CO_2Et and NH·CO_2Me, respectively).

The very ready cyclisation to the lactam (III) and the anomalous decompositions of the hydrazide (II; R = CO·NH·NH_2) spring from the increased basicity due to the replacement of an amino- by a methylamino-group in the 4-position of the pyrimidine nucleus; even so, this centre is still only weakly basic and it is surprising that it should be able so to dominate the reactions, though the decreased tendency of the substituted amino-compound to exist in the imino-form may also play a part. A sufficiently strong base can still reverse the reactions, however; thus, while the lactam (III) is unaffected by ammonia, it is cleaved by the stronger bases hydrazine and methylamine, to yield the corresponding hydrazide and methylamide.

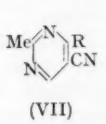
As an alternative route to the desired amine (II; R = NH_2), the intermediate 4-chloro-5-cyano-2-methylpyrimidine (VII; R = Cl) (Todd and Bergel, *J.*, 1937, 364) was prepared. It proved possible to introduce several modifications in this synthesis; thus ethyl α-cyano-α-ethoxymethyleneacetate was treated with two mols. of acetamidine instead of one, yielding the condensation product (VIII). This can be cyclised to 5-cyano-4-hydroxy-2-



(V)



(VI)



(VII)

H_2N·CMe:N·CH:C(CN)·CO·NH·CMe:NH

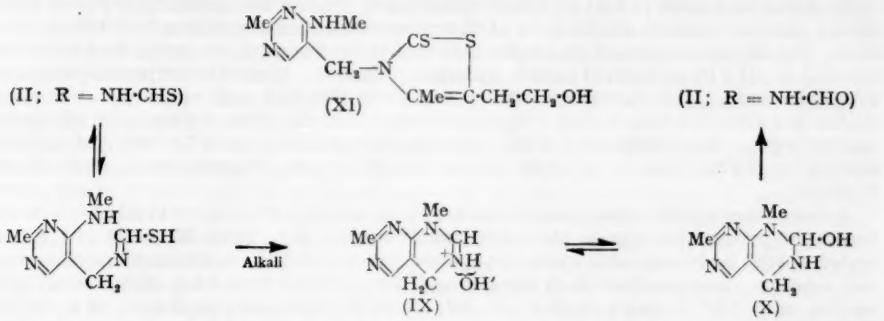
(VIII)

methylpyrimidine (VII; R = OH) which is then converted into the 4-chloro-compound with phosphorus oxychloride. Isolation of the hydroxypyrimidine or even separate cyclisation is unnecessary, however, as the crude condensation product can be converted directly into the chloro-compound in high yield. This is then converted into 5-cyano-2-methyl-4-methylaminopyrimidine (VII; R = NHMe) by adding it to liquid methylamine at −80° (higher temperatures lead to extensive side reactions). Catalytic hydrogenation of the cyano-compound to the amine (II; R = NH_2) proved unexpectedly difficult; the normal safeguards against secondary amine formation were ineffective, or inhibited reduction completely. The primary amine was obtained only if reduction was carried out in very dilute solution (<1%).

Treatment of the amine with sodium dithioformate led to the formyl derivative (II; R = NH·CHO) instead of the expected thioformyl compound (II; R = NH·CHS) (though the unstable thioformyl compound was obtained on one occasion only, being rapidly converted into the formyl derivative in solution or on attempted condensation with a chloro-ketone). Such an interconversion in the corresponding 4-amino-series (V; R′ = NH_2, R″ = NH·CHO and NH·CHS, respectively) can be effected only by heating an aqueous solution of the thioformyl compound in a sealed tube for several hours. It seems unlikely that the explanation of this difference is merely the greater basicity of the 4-methylamino-group as, under alkaline conditions, *N*-thioformyl compounds tend to be converted into the parent amine rather than that sulphur should be replaced by oxygen. The extreme readiness with which the 4-methylamino-group takes part in cyclisation reactions makes the formation of a cyclic intermediate such as (IX) not impossible, the corresponding *pseudo*-base (X) being a carbinol-amine corresponding to the formyl compound (II; R = NH·CHO). Such a cyclisation would certainly be promoted by the alkaline conditions prevailing during thioformylation.

Owing to the inability of this thioformyl compound (II; R = NH·CHS) to form *N*-methylthiamine (I) by reaction with a chloro-ketone, an alternative route from the amine

to (I) by formation of the 2-thione (XI), and its subsequent oxidation under acid conditions, was considered. Model compounds, such as (II; R = NH·CS·S·CH_2·COMe) were prepared but failed to undergo closure to the corresponding 2-thiones by Sykes's (*J.*, 1951, 2507) or Matsukawa's method (*J. Pharm. Soc. Japan*, 1951, **71**, 455). Here again it seems likely that the 4-methylamino-group is responsible, as a wide variety of 4-aminopyrimidine derivatives have been successfully cyclised by this method.



The desired vitamin analogue (I) was finally obtained in good yield by treatment of the hydrochloride of the formyl derivative (II; R = NH·CHO) with 3-acetoxy-1-chloropropyl methyl ketone in the presence of hydrogen sulphide.

Experimental

2-Methyl-4-methylamino-5-pyrimidylacetic Acid (II; R = CO_2H).—Ethyl 4-chloro-2-methyl-5-pyrimidylacetate (V; R′ = Cl, R″ = CO_2Et) (Cerecedo and Pickel, *J. Amer. Chem. Soc.*, 1937, **59**, 1714) (68 g.) was heated at 120° for 8 hr. with ethanolic methylamine (70 g. in 150 ml.). The ethanol was then removed, the residue dissolved in water (250 ml.), and a concentrated solution of barium hydroxide (100 g.) added. The solution was heated on a water-bath till no more methylamine could be detected, then treated with dilute sulphuric acid till no more barium sulphate was precipitated. The mixture was centrifuged and then evaporated under reduced pressure till crystallisation began. Recrystallisation from acetone–water gave 31 g. (54%) of colourless needles, m. p. 217° (Found: C, 53·0; H, 6·0; N, 23·2. Calc. for $C_8H_{11}O_2N_3$: C, 53·0; H, 6·1; N, 23·2%).

2-Methyl-4-methylaminopyrimidyl-5-acetolactam (1 : 6-*Dimethyl*-2-*oxo*-1 : 5 : 7-*triazaindane*) (III).—The above acid (30·9 g.) in ethanol (300 ml.) was refluxed for 6 hr. while dry hydrogen chloride was passed through the solution. The ethanol was removed, and the residue dissolved in ethanol and again evaporated to remove hydrochloric acid. This was repeated a second time and the residue set aside overnight in a vacuum-desiccator over solid potassium hydroxide. The residue was dissolved in ethanol, and concentrated aqueous sodium hydrogen carbonate (11·2 g., 1 equiv.) added. The solution was evaporated to small bulk and then freeze-dried. The residue was extracted with boiling alcohol, and the solution evaporated to dryness. Recrystallisation of the *lactam* from ethanol gave 15·3 g. (55%) of colourless needles, m. p. 141° (Found: C, 58·5; H, 5·5; N, 25·4. $C_8H_9ON_3$ requires C, 58·8; H, 5·5; N, 25·8%). Treatment of the lactam with ethanolic ammonia at 120° results in its recovery, while aqueous ammonia reconverts it into the acid. When the lactam was heated in acetone to which a little dry ammonia had been added, removal of the solvent and sublimation of the product at 150°/10^{-3} mm. gave the iso*propylidene* derivative (IV) as colourless needles, m. p. 172° (Found: C, 65·3; H, 6·4; N, 20·6%; *M*, 201. $C_{11}H_{13}ON_3$ requires C, 65·1; H, 6·4; N, 20·7%; *M*, 203).

Methyl 2-Methyl-4-methylamino-5-pyrimidylacetate (II; R = CO_2Me).—A suspension of the acid (2·9 g.) was stirred in ethanol (100 ml.) while excess of ethereal diazomethane was added and then until all the acid had passed into solution. Evaporation under reduced pressure at room temperature yielded the extremely unstable (it is converted overnight into a black tar) methyl ester, which decomposed on attempts at crystallisation, sublimation, etc. Reaction with ammonia converted it into the lactam (III).

2-Methyl-4-methylamino-5-pyrimidylacethydrazide (II; R = CO·NH·NH_2).—The above crude

methyl ester (freshly prepared from 3·76 g. of acid) was heated at 100° for 20 min. in aqueous hydrazine hydrate (50%; 20 ml.). Colourless crystals separated on cooling. Recrystallisation from ethanol gave 3·7 g. (92%) of colourless needles, m. p. 220° (Found: C, 49·5; H, 6·4; N, 35·8. $C_8H_{13}ON_5$ requires C, 49·2; H, 6·7; N, 35·9%). The *hydrazide* may also be obtained from the lactam (III) (79%) and the methylamide (II; R = CO·NHMe) (70%); it is unaffected by ammonia under any conditions tried.

1 : 2 : 3 : 4-*Tetrahydro*-1 : 7-*dimethyl*-2-*oxo*-1 : 3 : 6 : 8-*tetra-azanaphthalene* (VI).—A solution of the above hydrazide (7·5 g.) in N-hydrochloric acid (92 ml.) was cooled to −2° and stirred while a solution of sodium nitrite (2·7 g., 1·05 equivs.) was added dropwise and for 15 min. thereafter. The solution was heated on a water-bath until the evolution of gas ceased, then cooled and adjusted to pH 8 by addition of sodium hydrogen carbonate; it was then repeatedly extracted with chloroform. The chloroform extract was dried (Na_2SO_4) and evaporated. The solid residue was extracted with boiling anhydrous acteone, and the solution evaporated till crystallisation began. Recrystallisation of the *compound* from ethanol gave 4·7 g. (69%) of colourless needles, m. p. 222° (Found: C, 53·6; H, 5·5; N, 32·7. $C_8H_{10}ON_4$ requires C, 53·9; H, 5·6; N, 32·4%).

4-*Amino*-2-*methyl*-5-*pyrimidylacethydrazide* (V; R′ = NH_2, R″ = CO·NH·NH_2).—4-Amino-2-methyl-5-pyrimidylacetamide (Andersag and Westphal, *Ber.*, 1937, **70**, 2035) (4·1 g.) was heated at 100° for 30 min. with hydrazine hydrate (100%; 15 ml.); crystals separated from the cold solution. Recrystallisation of the *hydrazide* from ethanol gave 4·0 g. (89%) of colourless needles, m. p. 235° (Found: C, 46·6; H, 5·9; N, 38·7. $C_7H_{11}ON_5$ requires C, 46·4; H, 6·1; N, 38·7%).

4-*Amino*-5-*ethoxycarbonylaminomethyl*-2-*methylpyrimidine* (V; R′ = NH_2, R″ = NH·CO_2Et).—A suspension of the above hydrazide (1·025 g.) in ethanol (17 ml.), containing dry hydrogen chloride (0·413 g., 2 equivs.) and amyl nitrite (1·16 ml., 1 equiv.), was heated to 60° till gas evolution was complete. The solution was cooled and a large volume of ether added to precipitate the urethane hydrochloride, which was filtered off and dissolved in ethanol, and alcoholic sodium ethoxide solution (1·59N; 7·1 ml., 2 equivs.) was added. The mixture was then centrifuged to remove sodium chloride, and the resultant solution evaporated to crystallisation. Sublimation at 140°/10^{-4} mm. of the *ethylurethane* gave 0·28 g. (22%) of colourless needles, m. p. 214° (decomp.) (Found: C, 51·4; H, 6·9; N, 26·3. $C_9H_{14}O_2N_4$ requires C, 51·5; H, 6·7; N, 26·7%).

In methanol there was more rapid formation of the *methylurethane* (also purified by vacuum-sublimation) in 67% yield, m. p. 206° (Found: C, 49·2; H, 5·8; N, 28·4. $C_8H_{12}O_2N_4$ requires C, 48·9; H, 6·1; N, 28·5%).

N-(β-1-*Aminoethylideneamino*-α-*cyanoacryloyl*)*acetamidine* (VIII).—Acetamidine hydrochloride (166 g., 2·1 equivs.) was added to ethanolic sodium ethoxide (2·26N; 815 ml., 2·2 equivs.) at 0°, and the mixture shaken until all the acetamidine hydrochloride had dissolved, and then centrifuged to remove the precipitated sodium chloride. Ethyl α-cyano-α-ethoxymethyleneacetate (de Bollemont, *Bull. Soc. chim.*, 1901, **25**, 20) (141 g., 1 equiv.) at 60° was then added. The temperature rose rapidly to *ca.* 40°. The solution, which had become bright red, was left overnight at room temperature and then kept at 0° for 48 hr. The product separated as pale pink needles (more was obtained by concentraion of the mother-liquors, after filtration, and addition of ether). Recrystallisation of the *product* from ethanol gave 133 g. (83%) of colourless needles, m. p. 180° (Found: C, 48·3; H, 5·9; N, 34·7. $C_8H_{11}ON_5,\frac{1}{2}H_2O$ requires C, 48·5; H, 6·0; N, 34·7%).

5-*Cyano*-4-*hydroxy*-2-*methylpyrimidine* (VII; R = OH).—The foregoing compound (1·46 g.) in ethanol (10 ml.) and hydrochloric acid (0·5N; 15 ml., 1 equiv.) was heated to 100° for 10 min.; on cooling, crystals of the hydroxypyrimidine separated. This crystallised from water as colourless needles (0·69 g., 68%), m. p. 235° (Found: C, 52·9; H, 3·6; N, 31·0. Calc. for $C_6H_5ON_3$: C, 53·3; H, 3·7; N, 31·1%).

4-*Chloro*-5-*cyano*-2-*methylpyrimidine* (VII; R = Cl).—The crude amidine (VIII) (63 g.) was heated at 130°/4 mm. for 4 hr., the solid being shaken from time to time to prevent charring. After cooling, it was powdered and added to phosphorus oxychloride (1500 g.). The mixture was refluxed for 30 min. (air-bath), during which the amidine dissolved and the solution became dark red. The excess of phosphorus oxychloride was then removed under reduced pressure (it is extremely difficult to remove the last *ca.* 10%), and the warm flask then rotated so that the product solidified as a thin layer over the surface of the flask. The residue was then extracted with successive portions (300 ml. each) of ether, each portion being washed, as obtained, with potassium carbonate solution till neutral. These aqueous washings were then cooled

to 0° and added to the residue in the flask. The aqueous solution so obtained was neutralised with potassium carbonate and repeatedly ether-extracted. The ether extracts were combined with the original ether-washings and dried (Na_2SO_4) (*ca.* 4 l. of ether is required). The solvent was removed and the residue distilled, b. p. 79—81°/6 × 10^{-3} mm. The chloropyrimidine forms colourless needles (31 g., 62%), m. p. 64—65° (Found: C, 47·1; H, 3·0; N, 27·4. Calc. for $C_6H_4N_3Cl$: C, 46·9; H, 2·6; N, 27·4%).

5-Cyano-2-methyl-4-methylaminopyrimidine (VII; R = NHMe).—The above chloro-compound (32·3 g.) was finely powdered and added in 1-g. portions to liquid methylamine (250 ml.) cooled to −80°. The temperature, which rose to *ca.* −40° after each addition, was reduced to −80° again before the next addition. The excess of methylamine was then distilled off and the residue sublimed at 130°/10^{-3} mm. The *methylamino*-compound (20·6 g., 61%) was obtained as colourless needles, m. p. 151—152° (Found: C, 56·7; H, 5·3; N, 38·1. $C_7H_8N_4$ requires C, 56·7; H, 5·4; N, 37·8%).

Reduction of 5-Cyano-2-methyl-4-methylaminopyrimidine (VII; R = NHMe).—(*a*) The above methylaminocyano-compound (1·46 g.) in glacial acetic acid (200 ml.), saturated with hydrogen chloride, was hydrogenated at room temperature with 10% palladised charcoal as catalyst, the theoretical volume of hydrogen being absorbed in 2 hr. The mixture was diluted with water (200 ml.), filtered, and evaporated under reduced pressure. The residue was dissolved in water (10 ml.), the pH of the solution brought to 7 by the addition of sodium carbonate solution, and sodium dithioformate solution (2·1 g., 1 equiv.; in 10 ml.) added. No precipitate had formed after 3 days at room temperature, so the solution was extracted with chloroform, the extract dried (Na_2SO_4), the solvent removed under reduced pressure, and the residue sublimed at 140°/10^{-4} mm. Colourless needles (1·14 g., 64%) were obtained of 5-formamidomethyl-2-methyl-4-methylaminopyrimidine (II; R = NH·CHO), m. p. 152—153° (Found: C, 53·3; H, 6·6; N, 31·2. $C_8H_{12}ON_4$ requires C, 53·3; H, 6·7; N, 31·1%). Numerous attempts to repeat this reduction were unsuccessful.

(*b*) A solution of the methylaminocyanopyrimidine (0·78 g.) in acetic anhydride (100 ml.) containing triethylamine (0·74 ml., 1 equiv.) was hydrogenated at 35°/50 atm. with 10% palladised charcoal (0·3 g.). The mixture was filtered and then evaporated to dryness under reduced pressure. Triethylamine acetate was removed at room temperature at 10^{-4} mm. and the residue then sublimed at 10^{-4} mm., leading to recovery of starting material (0·113 g.) up to 100°, and from 120—140° sublimation of *5-acetamidomethyl-2-methyl-4-methylaminopyrimidine* (II; R = NHAc) (0·493 g., 52%), m. p. 213—214° (Found: C, 55·4; H, 7·3; N, 28·6. $C_9H_{14}ON_4$ requires C, 55·7; H, 7·2; N, 28·8%). Subsequent attempts resulted in the almost complete recovery of starting material. In the absence of triethylamine, a small amount of the acetamidomethyl compound is obtained, but the product is largely a mixture of acetamide and 5-acetoxymethyl-2-methyl-4-methylaminopyrimidine (II; R = OAc) arising from the decomposition of the secondary amine which is then the major product of the reduction of the cyanide.

Hydrolysis of 4-Amino-2-methyl-5-thioformamidomethylpyrimidine (V; R′ = NH_2, R″ = NH·CHS).—A solution of 4-amino-2-methyl-5-thioformamidomethylpyrimidine (Todd and Bergel, *J.*, 1937, 364) (0·19 g.) in water (15 ml.) was heated at 120° in a sealed tube for 2 hr. The solution, which had an odour of hydrogen sulphide, was freeze-dried and the residue sublimed at 140°/10^{-4} mm. The product (0·10 g., 60%) had m. p. 227—228°, undepressed on admixture with an authentic sample of 4-amino-5-formamidomethyl-2-methylpyrimidine (Andersag and Westphal, *Ber.*, 1937, **70**, 2035).

5-Aminomethyl-2-methyl-4-methylaminopyrimidine (II; R = NH_2).—A solution of the methylaminocyano-compound (1·00 g.) in *iso*propyl alcohol (200 ml.) was hydrogenated at room temperature and 6 atm. with freshly prepared W-7 Raney nickel (6 g.), the theoretical volume being absorbed in 1·5 hr. The mixture was then filtered through " Hyflo Supercel " and evaporated to dryness under reduced pressure. The yield of crude material was 0·75 g. (73%). Conversion into the acetyl compound with acetic anhydride–triethylamine, for characterisation, is almost quantitative.

2-Methyl-4-methylamino-5-thioformamidomethylpyrimidine (II; R = NH·CHS).—The above crude aminomethyl compound (0·89 g.) was dissolved in the minimum amount of methanol, and water (2 ml.) was added, followed by aqueous sodium dithioformate (1·34 g., 1·1 equivs.; in 10 ml.). After 2 days at room temperature the solution was concentrated to *ca.* 5 ml. under reduced pressure at room temperature. The *thioformyl* compound (0·68 g., 59%) separated as pale green needles, m. p. 132° (Found: C, 49·6; H, 6·2; N, 28·3. $C_8H_{12}N_4S$ requires C, 49·0; H, 6·2; N, 28·6%). Attempted recrystallisation gave the corresponding formyl compound, and other thioformylations of the aminomethyl compound also gave this as the major product.

Attempted condensation of the thioformyl compound with chloro-ketones resulted only in the formation of the hydrochloride, m. p. 234—235°, of the formyl compound.

5-*Formamidomethyl*-2-*methyl*-4-*methylaminopyrimidine Hydrochloride* (II; R = NH·CHO).—The crude aminomethylmethylaminopyrimidine (from 4·06 g. of the cyano-compound) was refluxed in formic acid (98%; 20 ml.) for 6 hr. The solution was evaporated to dryness, the residue dissolved in water, and the pH of the solution brought to 7 by the addition of aqueous potassium carbonate solution. The solution was extracted with butanol, and the butanol extract dried (Na_2SO_4) and evaporated to dryness under reduced pressure. The residue was dissolved in acetone, and ethanolic hydrogen chloride (10%) added, followed by a trace of ether. After being kept overnight at 0° the colourless crystals were filtered off. Recrystallisation from ethanol–ether yielded colourless needles (3·23 g., 54%) of the *hydrochloride*, m. p. 234—235°, of the formyl compound (Found: C, 44·3; H, 5·9; N, 25·8. $C_8H_{12}ON_4$,HCl requires C, 44·3; H, 6·0; N, 25·8%).

S-*Acetonyl* N-(2-*Methyl*-4-*methylamino*-5-*pyrimidylmethyl*) *Dithiocarbamate* (II; R = NH·CS·S·CH_2·COMe).—A solution of the crude aminomethyl compound (from 0·97 g. of the cyano-compound) in methanol (10 ml.) and water (3 ml.) was treated with potassium hydroxide (0·37 g.) in methanol (6 ml.) and water (2 ml.), followed by carbon disulphide (0·40 ml.). The mixture was vigorously shaken for 15 min.; chloroacetone (0·52 ml.) was then added and shaking continued for a further 30 min. The precipitated potassium chloride (0·28 g., 57%) was then filtered off and the solution diluted with water (10 ml.). Crystals were deposited from the solution at 0°. Recrystallisation from methanol followed by sublimation at 140°/10^{-4} mm. led to colourless needles (0·51 g., 27%) of the *dithiocarbamate*, m. p. 242—243° (Found: C, 46·7; H, 5·4; N, 20·0. $C_{11}H_{16}ON_4S_2$ requires C, 46·4; H, 5·6; N, 19·7%). Heating the solid to 100°, or refluxing a solution of the compound in hydrochloric acid (10%), failed to effect the desired cyclisation (cf. Sykes, *J.*, 1951, 2507), the starting material being recovered.

5-2′-*Hydroxyethyl*-4-*methyl*-3-(2-*methyl*-4-*methylamino*-5-*pyrimidylmethyl*)*thiazolium Chloride Hydrochloride* (N-*Methylthiamine Chloride Hydrochloride*) (I).—5-Formamidomethyl-2-methyl-4-methylaminopyrimidine hydrochloride (13·8 g.) was added to a mixture of formic acid (16·5 ml.), activated charcoal (2 g.), and 3-acetoxy-1-chloropropyl methyl ketone (12 g.), and hydrogen sulphide was passed through the mixture at 115—120° for 5 hr. The solution was then evaporated to dryness under reduced pressure and kept over solid potassium hydroxide (pellets) in a vacuum-desiccator overnight. The residue was then extracted with boiling methanol, decolorised with activated charcoal, filtered, and diluted with ether. Crystals separated when the solution was left at 0°. A further crop was obtained on concentration of the mother liquors and treatment with more ether. Recrystallisation from methanol–ether yielded colourless needles (10·7 g., 48%) of *N*-methylthiamine chloride hydrochloride, m. p. 253—254° (Found: C, 44·7; H, 5·7; N, 16·0. Calc. for $C_{13}H_{20}ON_4SCl_2$: C, 44·5; H, 5·7; N, 16·0%).

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Survey of Anthoxanthins. Part VI. Colouring Matter of* Tamarix troupii. *Constitution of the Aglycone and its Synthesis.*

By S. R. Gupta and T. R. Seshadri.

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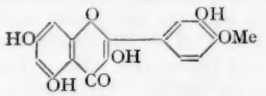
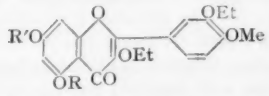
The green leaves of *Tamarix troupii* contain a glycoside, tamarixin, of a new flavonol, whose constitution is established as 3 : 5 : 7 : 3′-tetrahydroxy-4′-methoxyflavone and confirmed by synthesis.

Tamarix troupii is an ornamental plant, parts of which find use in medicine and in tanning. From the dried leaves of *T. gallica* and *T. africana* Perkin and Wood (*J.*, 1898, **73**, 374) isolated ellagic acid and a trace of a yellow flavonol which was considered to be a monomethyl ether of quercetin, different from rhamnetin and *iso*rhamnetin; they, however, were not sure about its purity.

Fresh leaves of *T. troupii*, collected in Delhi, have now been examined: drying brings about adverse changes, and extraction becomes difficult. The colouring matter is a single entity, as shown by paper chromatography. It is a flavonol glycoside, now termed tamarixin. The aglycone, $C_{16}H_{12}O_7$, contains one methoxyl group: on demethylation it yields quercetin, on partial methylation yields quercetin tetramethyl ether (5-hydroxy-3 : 7 : 3′ : 4′-tetramethoxyflavone), and on complete methylation yields quercetin pentamethyl ether. Consequently the methoxyl group is not in position 5. The flavone differs from rhamnetin, *iso*rhamnetin, and quercetin 3-methyl ether (recently prepared in this laboratory; unpublished work); it should therefore be the hitherto unknown 4′-methyl ether (I).

This constitution was confirmed as follows: the aglycone was fully ethylated and the ethyl ether subjected to fission with alcoholic potassium hydroxide, which gave 3-ethoxy-4-methoxybenzoic acid (obtained by the ethylation of *iso*vanillic acid) and ω : 4 : 6-triethoxy-2-hydroxyacetophenone (Perkin, *J.*, 1912, **101**, 329; Row and Seshadri, *Proc. Indian Acad. Sci.*, 1946, **23**, *A*, 140). Ethylation had thus given 3 : 5 : 7 : 3′-tetraethoxy-4′-methoxyflavone (II). This was synthesised by condensing ω-ethoxyphloracetophenone (Row and Seshadri, *loc. cit.*) with the anhydride and the potassium salt of 3-ethoxy-4-methoxybenzoic acid and subjecting the resulting product (III) to further ethylation.

(I) 



(II; R = R′ = Et)

(III; R = R′ = H)

The aglycone (I) has also been synthesised by partial demethylation of quercetin 3 : 4′-dimethyl ether (King, King, and Sellars, *J.*, 1952, 92) as in the analogous synthesis of rhamnazin and kaempferide (Rao and Seshadri, *J.*, 1946, 771; 1947, 122).

Experimental

Extraction.—The fresh leaves (1200 g.) were extracted twice with boiling alcohol, each time for 8 hr. The dark green extract (6 l.) was concentrated under reduced pressure; chlorophyll and waxes separated and were filtered off. The concentrate was repeatedly extracted with light petroleum (b. p. 45—65°), the remaining wax and the green colouring matter being removed. The residual dark brown solution was extracted with ether; the ether extract did not contain any aglycone. An almost colourless solid separated as a fine powder from the aqueous layer. It was filtered off, washed successively with water, alcohol, and ether, and dried (yield, 1·5 g.). The filtrate contained mainly tannins and no anthoxanthins and was discarded. In chromatography (horizontal migration) in which the upper layer of butanol–acetic acid–water (4 : 1 : 5) was used, the solid product gave a single ring (R_F 0·71 at 29—30°). After crystallisation from hot water and from alcohol–water tamarixin was obtained as rectangular prisms, m. p. 315—317° (decomp.). It has not, however, been obtained free from mineral impurities. It is easily soluble in hot water and sparingly soluble in alcohol and other organic solvents.

* Part V, *J. Sci. Ind. Res., India*, 1954, **13**, *B*, 475.

The Aglycone.—Tamarixin (0·5 g.) was refluxed with 7% sulphuric acid (75 c.c.). Though separation of the aglycone started after 15 min., heating was continued for 2 hr. to ensure complete hydrolysis. The mixture was cooled, and the aglycone filtered off and washed with water. More was obtained by extracting the filtrate with ether and evaporating the ether extract, the total yield being 0·31 g. (62%). It has R_F 0·85 in phenol–water (lower layer) at 30°. The *aglycone* crystallised from aqueous alcohol as bright golden-yellow rectangular prisms, m.p. 259—260°. It was insoluble in water, but dissolved readily in alcohol, ether, and acetone. In alcoholic solution it gave an olive-brown colour with ferric chloride, an orange lead salt with neutral and basic lead acetates, and a red colour with magnesium and hydrochloric acid. It gave no colour with zinc and hydrochloric acid (Pew's test), and dissolved in concentrated sulphuric acid to a golden-yellow solution with green fluorescence, and in aqueous sodium hydroxide (1%) and sodium carbonate (5%) to yellow solutions (Found: C, 57·9; H, 4·3; OMe, 9·1. $C_{16}H_{12}O_7,H_2O$ requires C, 57·3; H, 4·2; 1OMe, 9·3%). The *acetyl* derivative crystallised from alcohol as colourless prismatic needles and rods, m. p. 203—204° (Found: C, 59·4; H, 4·3. $C_{24}H_{20}O_{11}$ requires C, 59·5; H, 4·1%).

Methylation of the Aglycone.—(*a*) The aglycone (0·2 g.) in anhydrous acetone (30 c.c.) was refluxed with methyl sulphate (0·22 c.c., 3·2 mols.) and anhydrous potassium carbonate (2 g.) for 10 hr. The methyl ether obtained after removal of the solvent from the filtrate crystallised from ethyl alcohol as pale yellow needles (0·21 g.), m. p. 159—160°. Herzig (*Monatsh.*, 1888, **9**, 541; 1912, **33**, 690) gave the same m. p. for 5-hydroxy-7 : 3 : 3′ : 4′-tetramethoxyflavone. Its alcoholic solution gave a brown colour with ferric chloride.

(*b*) The aglycone (0·2 g.), anhydrous acetone (25 c.c.), excess of methyl sulphate (1 c.c.), and ignited potassium carbonate (3 g.) were refluxed for 50 hr. The product crystallised from alcohol (charcoal) as colourless needles, m. p. 151—152° alone or mixed with quercetin pentamethyl ether.

Demethylation of the Aglycone.—The aglycone (0·5 g.) was heated with acetic anhydride (10 c.c.) and hydriodic acid (10 c.c.) at 145—150° for 2 hr. The cooled mixture was diluted with aqueous sodium hydrogen sulphite, a yellow flocculent precipitate separating, which crystallised from dilute alcohol as yellow needles, m. p. 314—315° (decomp.), alone or mixed with quercetin. With acetic anhydride and pyridine this gave quercetin penta-acetate, needles (from alcohol–benzene), m. p. and mixed m. p. 193—195°.

Ethylation of the Aglycone.—The aglycone (0·3 g.), anhydrous acetone (50 c.c.), ethyl sulphate (excess, 1 c.c.), and ignited potassium carbonate (3 g.) were refluxed for 50 hr. The *tetraethyl ether* crystallised from alcohol as stout prisms, m. p. 136—137° (0·35 g.) (Found: C, 67·3; H, 6·6. $C_{24}H_{28}O_7$ requires C, 67·3; H, 6·5%).

Alkali Fission of the Ethyl Ether.—The ethyl ether (0·3 g.) was heated with alcoholic (8%) potassium hydroxide (30 c.c.). The substance dissolved and soon an orange-red crystalline solid was deposited. After 6 hours' refluxing, the solvent was distilled off, the residue dissolved in water (20 c.c.), and the clear solution acidified and extracted thrice with ether. The ether extract was repeatedly shaken with aqueous sodium hydrogen carbonate. Acidification of the carbonate extract gave colourless *O*-ethyl*iso*vanillic acid, needles, m. p. and mixed m. p. 165—166° (from dilute alcohol).

The remaining ether solution on evaporation gave a small quantity of brown solid, which crystallised from ether–light petroleum as flat needles and plates, m. p. 97—98°. The same m. p. has been recorded for ω : 4 : 6-triethoxy-2-hydroxyacetophenone (Perkin; Row and Seshadri, *locc. cit.*).

For comparison *iso*vanillic acid was obtained as follows: Methyl protocatechuate (18·2 g.) in dry acetone (150 c.c.) was heated with methyl sulphate (10 c.c., 1 mol.) and ignited potassium carbonate (25 g.) for 3 hr. The potassium salts were filtered off and washed with hot acetone. The solvent from the filtrate was then removed by distillation, the residue treated with water, and the colourless solid that separated was filtered off and washed with water. The ether ester so obtained was refluxed with aqueous sodium hydroxide (10%; 150 c.c.) for 2 hr., and then acidified with hydrochloric acid. *iso*Vanillic acid, which separated, crystallised from alcohol as colourless prisms, m. p. 255—257° (13 g.). This acid (16·8 g.) was refluxed with ethyl sulphate (38·5 g.; 2·5 mols.) and potassium carbonate (80 g.) in anhydrous acetone (150 c.c.) for 10 hr. and the resulting ether ester hydrolysed by boiling 10% aqueous sodium hydroxide. *O*-Ethyl*iso*vanillic acid crystallised from dilute alcohol as colourless needles, m. p. 165—166° (15 g.). Its anhydride was prepared by adding a solution of thionyl chloride (2 c.c.) in ether (25 c.c.) with stirring to a suspension of powdered *O*-ethyl*iso*vanillic acid (9·8 g.) in dry ether (40 c.c.) and pyridine (4 c.c.) cooled in ice–salt. The whole was kept in the refrigerator overnight. Crushed

ice was then added, and the solid was collected, triturated successively with ice-cold dilute hydrochloric acid, dilute aqueous sodium hydrogen carbonate, and water, and dried in a vacuum desiccator. The *anhydride* crystallised from dry benzene as colourless prisms, m. p. 149—150° (7·5 g.) (Found: C, 63·9; H, 6·1. $C_{20}H_{22}O_7$ requires C, 64·2; H, 5·9%).

3 : 3′-*Diethoxy*-5 : 7-*dihydroxy*-4′-*methoxyflavone* (III).—An intimate mixture of ω-ethoxyphloracetophenone (0·4 g.), the anhydride (2·5 g.), and the potassium salt (0·8 g.) of *O*-ethyl-*iso*vanillic acid was heated at 170—180° under reduced pressure for 3 hr. The cooled product was dissolved in ethyl alcohol (20 c.c.), water (2 c.c.) containing potassium hydroxide (2·8 g.) was added, and the solution boiled for 20 min. The solvents were then removed under reduced pressure and water was added. The aqueous solution was extracted once with ether and then saturated with carbon dioxide, and the precipitated *flavone* was collected and crystallised from alcohol, forming prismatic needles, m. p. 183—185° (0·5 g.). Its alcoholic solution gave a reddish-brown colour with ferric chloride (Found, after drying *in vacuo* at 110°: C, 64·4; H, 5·4. $C_{20}H_{20}O_7$ requires C, 64·5; H, 5·4%).

5 : 7 : 3 : 3′-*Tetraethoxy*-4′-*methoxyflavone* (II).—The above diethoxyflavone (0·3 g.) was ethylated with ethyl sulphate (0·4 c.c.) and potassium carbonate (2 g.) in boiling anhydrous acetone (50 c.c.) for 30 hr. The tetraethyl ether crystallised from alcohol as stout prisms, m. p. 136—137° (0·28 g.), gave a negative ferric reaction, and was insoluble in aqueous sodium hydroxide. This was found to be identical with the aglycone tetraethyl ether (mixed m. p.).

5 : 7 : 3 : 3′-*Tetrahydroxy*-4′-*methoxyflavone* (I).—5 : 7 : 3′-Trihydroxy-3 : 4′-dimethoxyflavone (King *et al.*, *loc. cit.*) (0·5 g.) was dissolved in dry nitrobenzene (4 c.c.), treated with a solution of anhydrous aluminium chloride (1 g.) in the same solvent (4 c.c.), and kept in a boiling-water bath for 1½ hr. The mixture was then cooled and excess of light petroleum added. The brown precipitate was filtered off and washed with light petroleum. It was then treated with dilute hydrochloric acid, the mixture was heated nearly to boiling and filtered, and the solid residue washed with water. The product (0·4 g.) crystallised from dilute alcohol as rectangular prisms m. p. and mixed m. p. 259—260°. The acetyl derivative crystallised from alcohol as prismatic needles and rods, m. p. and mixed m. p. 203—204°.

Our thanks are due to Dr. S. K. Mukerjee for microanalysis.

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Nuclear Oxidation in Flavones and Related Compounds. Part XLVII. A New Synthesis of Fraxetin and a Synthesis of 4-Methylfraxetin.*

By K. Aghoramurthy and T. R. Seshadri.

[Reprint Order No. 5294.]

A new and convenient synthesis of fraxetin and 4-methylfraxetin has been carried out from 8-acetyl-7-methoxycoumarin and its 4-methyl derivative respectively, by nuclear oxidation in the 6-position followed by methylation to yield 8-acetyl-6 : 7-dimethoxy-compounds, partial demethylation in the 7-position, and final Dakin oxidation.

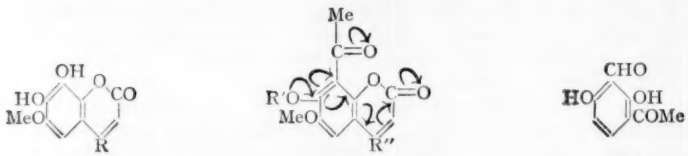
Späth and Dobrovolny (*Ber.*, 1938, **71**, 1831) synthesised fraxetin (I; R = H) in a small yield by condensing 2 : 3 : 4-trihydroxy-1-methoxybenzene with formylacetic ester; and Späth and Schmid (*Ber.*, 1941, **74**, 598) converted scopoletin through its 8-aldehyde into fraxetin, but the yield of aldehyde was very poor. Since use of a ketone might have been better than that of an aldehyde, Fries rearrangement of scopoletin acetate was attempted under different conditions (Baker and Evans, *J.*, 1938, 374; Lohfert and Rosenmund, *Ber.*, 1928, **61**, 2601), but was unsuccessful. Hence alternative routes to 8-acetyl-7-hydroxy-6-methoxycoumarin (II; R′ = R″ = H) have been explored.

First, 8-acetyl-7-methoxy-4-methylcoumarin (Limaye and Sathe, *Rasayanam*, 1936, **1**, 35) was subjected to persulphate oxidation, to give 8-acetyl-6-hydroxy-7-methoxy-4-methylcoumarin in over 50% yield. 8-Acetyl-4-methylumbelliferone similarly yielded

* Part XLVI, *Proc. Indian Acad. Sci.*, 1953, **38**, *A*, 480.

8-acetyl-6 : 7-dihydroxy-4-methylcoumarin (25% yield), but partial methylation of this dihydroxy-compound was unsuccessful. However, after initial failures, partial demethylation of 8-acetyl-6 : 7-dimethoxy-4-methylcoumarin (II; R′ = R″ = Me) by concentrated sulphuric acid gave good yields of 8-acetyl-7-hydroxy-6-methoxy-4-methylcoumarin. The product (m. p. 193—194°) was different from that reported by Baker and Evans (*loc. cit.*) (m. p. 250°). Its constitution was established by converting it into 4-methylfraxetin (I; R = Me) by Dakin oxidation and finally into the known 6 : 7 : 8-trihydroxy- and -trimethoxy-4-methylcoumarin.

Though concentrated sulphuric acid is known to bring about demethylation, it has not been considered suitable for the partial demethylation of a methoxyl group situated *ortho* to a carbonyl; but the reagent of common choice, aluminium chloride, failed in the present case. In view of the analogy of partial demethylation, by sulphuric acid, of trimethylgallic acid to syringic acid (Bogert and Coyne, *J. Amer. Chem. Soc.*, 1929, **51**, 569), it could be suggested that demethylation of the 7-methoxyl group is encouraged by the unsaturated



(I) (II) (III)

carbonyl system of the α-pyrone (see II). However this influence alone is not enough since 7-methoxycoumarin does not suffer demethylation under the same conditions whereas 8-acetyl-7-methoxycoumarin is demethylated. Obviously the carbonyl group in the 8-position is also necessary.

The marked solubility of these 8-acetyl-7-hydroxycoumarins in aqueous sodium carbonate seems to be due also to the combined influence of electron-attracting groups in both the *ortho*- and the *para*-position. A closely related example is 3-formyl-2 : 4-dihydroxyacetophenone (III) which is also readily soluble in aqueous sodium hydrogen carbonate.

Fraxetin (I; R = H) has been synthesised similarly in satisfactory yield, starting from 8-acetyl-7-methoxycoumarin.

Experimental

8-Acetyl-6-hydroxy-7-methoxy-4-methylcoumarin.—8-Acetyl-7-methoxy-4-methylcoumarin (Limaye and Sathe, *loc. cit.*) (11 g.) was heated with aqueous sodium hydroxide (10%; 100 c.c.) at 100° for 1 hr. The solution was treated at 10° with stirring during 6 hr. with aqueous potassium persulphate (5%; 300 c.c.), the mixture was kept at room temperature for 24 hr. and acidified to Congo-red, and the precipitated solid (unchanged coumarin) was filtered off. The filtrate was extracted with ether thrice to remove unchanged coumarin (4 g.). The aqueous layer was treated with concentrated hydrochloric acid (80 c.c.) and sodium sulphite (2 g.) and heated for 2 hr. on a boiling-water bath and cooled. *8-Acetyl-6-hydroxy-7-methoxy-4-methylcoumarin* that separated crystallised from dilute alcohol as colourless rhombohedral tablets, m. p. 242—243° (4 g.) (Found: C, 62·9; H, 4·9. $C_{13}H_{12}O_5$ requires C, 62·9; H, 4·8%). The methyl ether, prepared by methyl sulphate–acetone–potassium carbonate, crystallised from alcohol as colourless elongated rectangular plates and prisms, m. p. 115—116°. It exhibited a strong bluish-green fluorescence in dry ether solution.

8-Acetyl-6 : 7-dihydroxy-4-methylcoumarin.—8-Acetyl-4-methylumbelliferone (Limaye and Sathe, *loc. cit.*) (10 g.) in aqueous sodium hydroxide (10%; 100 c.c.), oxidised as above with aqueous potassium persulphate (5%; 300 c.c.), yielded the unchanged compound (2 g.) and *8-acetyl-6 : 7-dihydroxy-4-methylcoumarin* (2 g.). The latter, pale yellow plates (from alcohol), m. p. 220—222°, gave a deep green colour with alcoholic ferric chloride and quickly dissolved to a yellow solution in aqueous sodium carbonate (Found: C, 61·2; H, 4·5. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3%).

8-Acetyl-7-hydroxy-6-methoxy-4-methylcoumarin (II; R′ = H, R″ = Me).—A solution of

8-acetyl-6 : 7-dimethoxy-4-methylcoumarin (1 g.) in sulphuric acid (6 c.c.; *d* 1·8) was kept at 30° for 24 hr. and then poured into water (100 c.c.) without cooling. The solid that separated crystallised from alcohol as long yellow rectangular rods and prisms, m. p. 193—194°. The *coumarin* gave a reddish brown colour with alcoholic ferric chloride and was soluble in aqueous sodium carbonate (Found : C, 63·1; H, 4·8%).

4-Methylfraxetin (I; R = Me).—A solution of the preceding acetylcoumarin (1 g.) in N-sodium hydroxide (6 c.c.) at 0° was treated with hydrogen peroxide (30 c.c.; 20-vol.) all at once. The temperature rose and soon a crystalline solid separated. After 1 hr. at room temperature *4-methylfraxetin* was filtered off. It crystallised from alcohol–benzene as colourless rhombohedral tablets, m. p. 260—261° (0·5 g.) (Found : C, 59·9; H, 5·0. $C_{11}H_{10}O_5$ requires C, 59·5; H, 4·5%). It gave a bluish-green colour with alcoholic ferric chloride and did not fluoresce in alkaline solutions. It dissolved quickly in aqueous sodium carbonate to a yellow solution. The diacetate crystallised from alcohol–benzene as colourless needles, m. p. 220—221°.

6 : 7 : 8-*Trihydroxy-4-methylcoumarin.*—4-Methylfraxetin (0·5 g.) in acetic anhydride (5 c.c.) and hydriodic acid (10 c.c.; *d* 1·7) was refluxed for 1 hr., then poured into water, and the free iodine removed by sulphur dioxide. The solid crystallised from alcohol–benzene as colourless rectangular tablets, m. p. 278° (decomp.). Oliverio and Baroni (*Gazzetta*, 1949, **79**, 906) gave m. p. 282°; Parikh and Sethna (*J. Indian Chem. Soc.*, 1950, **27**, 369) gave m. p. 276°. The trihydroxycoumarin gave a blue colour with ferric chloride solution and a deep yellow solution with alkali which became brown in air. The triacetate crystallised from alcohol–benzene as colourless needles, m. p. 143°. The trimethyl ether prepared by methyl sulphate–acetone–potassium carbonate crystallised from dilute alcohol as colourless needles, m. p. 114°. Oliverio *et al.* (*loc. cit.*) gave the same m. p. for the derivatives.

8-Acetyl-6-hydroxy-7-methoxycoumarin.—8-Acetyl-7-methoxycoumarin (Limaye and Joshi, *Rasayanam*, 1941, **1**, 227) (2·2 g.) was dissolved in aqueous potassium hydroxide (14%; 20 c.c.) by heating at 100° for 1 hr. and oxidised as described above with aqueous potassium persulphate (3%; 100 c.c.). *8-Acetyl-6-hydroxy-7-methoxycoumarin* crystallised from alcohol as plates, m. p. 196—197° (0·8 g.) (Found : C, 61·1; H, 3·9. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3%). The methyl ether, prepared as above, crystallised from dilute alcohol as rectangular prisms, m. p. 94—95°.

8-Acetyl-7-hydroxy-6-methoxycoumarin (II; R′ = R″ = H).—The dimethyl ether (0·6 g.) was kept in sulphuric acid (2·5 c.c.; *d* 1·8) at 30° for 24 hr., then poured into water (50 c.c.) without cooling. The *acetylcoumarin* crystallised from alcohol as pale yellow thin rectangular plates, m. p. 180° (0·4 g.), soluble in sodium carbonate solution and giving a reddish-brown colour with alcoholic ferric chloride (Found : C, 61·6; H, 4·4%).

Fraxetin (I; R = H).—The above acetylhydroxycoumarin (0·4 g.) in N-sodium hydroxide (2·5 c.c.) was oxidised by hydrogen peroxide (25 c.c.; 20-vol.). Fraxetin crystallised from alcohol–benzene as plates, m. p. 227—228° (0·2 g.), giving a bluish-green colour with alcoholic ferric chloride (Found : C, 57·8; H, 4·3. Calc. for $C_{10}H_8O_5$: C, 57·7; H, 3·8%). The diacetate crystallised from alcohol–benzene as prisms, m. p. 192—193°. Simada (*J. Pharm. Soc. Japan*, 1937, **57**, 148) gave the same m. p.

8-Acetyl-7-hydroxycoumarin.—8-Acetyl-7-methoxycoumarin (0·5 g.) was demethylated with sulphuric acid (2·5 c.c.; *d* 1·8). 8-Acetyl-7-hydroxycoumarin (0·2 g.) crystallised from alcohol as pale yellow needles, m. p. and mixed m. p. 167°. It was soluble in aqueous sodium carbonate and gave a violet colour with alcoholic ferric chloride.

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Preparation of Tetrahydro-1 : 4-thiazine 1 : 1-Dioxides.

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Sulphonyldiacetic acid and its ethyl and methyl esters, when condensed with aromatic aldehydes and ammonia or aliphatic primary amines, give substituted tetrahydro-1 : 4-thiazine 1 : 1-dioxides.

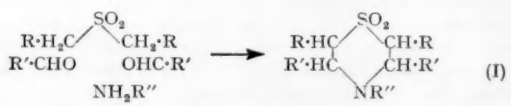
By analogy with the well-known condensation of acetonedicarboxylic esters or ketones with aromatic aldehydes and ammonia or certain aliphatic amines to give 4-piperidones, it might be expected that sulphones might yield tetrahydro-1 : 4-thiazine 1 : 1-dioxides (I). Failure of sulphones to condense thus was reported by Balasubramanian and Baliah (*J.*, in the press), it being probable that the α-hydrogen atoms are not sufficiently labile. However, diethyl sulphonyldiacetate, in which the methylene groups are activated by ethoxycarbonyl as well as by sulphonyl groups, condensed with a variety of aldehydes and ammonia or amines, giving excellent yields of the thiazine derivatives listed in Table 1.

TABLE 1. *Substituted tetrahydro-1 : 4-thiazine 1 : 1-dioxides* (I; R = CO_2Et).

R′	R″	Yield (%)	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
Ph	H	83	184—185°	$C_{22}H_{25}O_6NS$	61·2	5·8	61·2	5·8
p-MeO·C_6H_4	H	57	171—173	$C_{24}H_{29}O_8NS$	58·3	5·6	58·6	5·9
o-MeO·C_6H_4	H	73	140—141	$C_{24}H_{29}O_8NS$	58·5	5·7	58·6	5·9
3 : 4-CH_2O_2·C_6H_3	H	67	216—218	$C_{24}H_{25}O_{10}NS$	55·4	4·7	55·5	4·9
3 : 4-MeO(OH)C_6H_3 [a]	H	46	185—187	$C_{24}H_{29}O_{10}NS$	55·0	5·3	55·0	5·6
p-Cl·C_6H_4	H	95	209—210	$C_{22}H_{23}O_6NCl_2S$	52·6	4·9	52·8	4·6
o-Cl·C_6H_4	H	63	143—145	$C_{22}H_{23}O_6NCl_2S$	52·5	4·9	52·8	4·6
m-O_2N·C_6H_4	H	87	183—184	$C_{22}H_{23}O_{10}N_3S$	50·6	4·3	50·7	4·4
o-O_2N·C_6H_4 [b]	H	73	198—199	$C_{22}H_{23}O_{10}N_3S$	50·6	4·5	50·7	4·4
p-Me·C_6H_4	H	65	169—171	$C_{24}H_{29}O_6NS$	62·9	6·4	62·7	6·4
2-Thienyl	H	54	158—159	$C_{16}H_{21}O_6NS_3$	48·4	4·8	48·7	4·8
3 : 4-$(MeO)_2C_6H_3$	H	46	160—162	$C_{26}H_{33}O_{10}NS$	56·6	6·2	56·6	6·0
Ph	Me	76	205—207	$C_{23}H_{27}O_6NS$	61·8	5·7	62·0	6·1
Ph	Et	73	199—201	$C_{24}H_{29}O_6NS$	63·1	6·3	62·7	6·4
Ph	Allyl	51	165—167	$C_{25}H_{29}O_6NS$	63·5	6·1	63·7	6·2
Ph	Bu^n	34	141—142	$C_{26}H_{33}O_6NS$	64·3	6·8	64·1	6·8
Ph	*n*-C_8H_{17}	35	120—121	$C_{30}H_{41}O_6NS$	66·0	7·4	66·3	7·6
Ph	C_6H_5·CH_2	58	159—161	$C_{29}H_{31}O_6NS$	66·9	5·8	66·8	6·0

[a] Rhombic crystals from dioxan–water. [b] Pale yellow needles from acetone–ethanol.

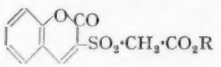
In ether or benzene these compounds form hydrochlorides which in water regenerate the bases and cannot be recrystallised.



(I)

Only aliphatic amines undergo the condensation; the yields decrease with the higher homologues.

Only aromatic aldehydes undergo this condensation, *p*-chlorobenzaldehyde being the most reactive of those tried. No condensation occurred with *m*-hydroxy-, *p*-hydroxy-, or 2 : 4-dinitro-benzaldehyde. Salicylaldehyde gave a monocoumarin derivative (II; R = Et), and cinnamaldehyde gave only the unsaturated sulphone (III) (Backer, *Rec. Trav. chim.*, 1953, **72**, 119). Of aliphatic aldehydes investigated, only formaldehyde reacted and that gave only an unidentified product.

(II)  [C_6H_5·CH:CH·CH:C(CO_2Et)–]$_2SO_2$ (III)

Dimethyl sulphonyldiacetate reacted as well as the ethyl ester, and the compounds

prepared from it are given in Table 2. Salicylaldehyde gave 3 : 3′-dicoumarinylsulphone (IV) as well as the monocoumarin (II; R = Me).

TABLE 2. *Substituted tetrahydro*-1 : 4-*thiazine* 1 : 1-*dioxides* (I; R = CO_2Me).

R′	R″	Yield (%)	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
Ph	H	62	219—221°	$C_{20}H_{21}O_6NS$	59·8	5·0	59·6	5·2
3 : 4-CH_2O_2:C_6H_3 [a]	H	82	225—226	$C_{22}H_{21}O_{10}NS$	53·6	4·3	53·8	4·3
3 : 4-MeO(OH)C_6H_3 [b]	H	40	204—206	$C_{22}H_{25}O_{10}NS$	53·5	5·3	53·3	5·2
m-O_2N·C_6H_4 [c]	H	83	205—207	$C_{20}H_{19}O_{10}N_3S$	48·7	4·0	48·7	3·9
o-O_2N·C_6H_4 [c]	H	54	210—211	$C_{20}H_{19}O_{10}N_3S$	48·8	3·8	48·7	3·9
p-Me·C_6H_4	H	39	203—205	$C_{22}H_{25}O_6NS$	61·2	5·8	61·2	5·8
2-Thienyl	H	77	177—178	$C_{16}H_{17}O_6NS_3$	46·7	4·0	46·3	4·1
p-Cl·C_6H_4	H	91	220—221	$C_{20}H_{19}O_6NCl_2S$	51·1	4·4	50·9	4·1
o-Cl·C_6H_4	H	73	174—176	$C_{20}H_{19}O_6NCl_2S$	50·7	4·2	50·9	4·1
3 : 4-$(MeO)_2C_6H_3$	H	64	173—174	$C_{24}H_{29}O_{10}NS$	54·8	5·3	55·1	5·6
Ph [d]	Allyl	54	163—164	$C_{22}H_{25}O_6NS$	62·0	5·7	62·3	5·7
m-O_2N·C_6H_4 [c]	Et	32	239—241	$C_{22}H_{23}O_{10}N_3S$	51·0	4·8	50·7	4·4

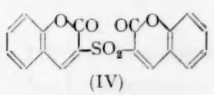
[a] Needles from acetone–ethanol. [b] Needles from dioxan–water. [c] Pale yellow needles from acetone–ethanol. [d] Softens at 129°.

TABLE 3. 3 : 5-*Diaryltetrahydro*-1 : 4-*thiazine* 1 : 1-*dioxides* (V).

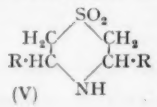
R	Yield (%)	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
Ph	34	205—206°	$C_{16}H_{17}O_2NS$	67·2	5·9	66·9	6·0
p-MeO·C_6H_4	40	210—212	$C_{18}H_{21}O_4NS$	62·0	5·8	62·2	6·1
p-Me·C_6H_4	30	168—170	$C_{18}H_{21}O_2NS$	69·0	6·8	68·6	6·7
p-Cl·C_6H_4	52	194—195	$C_{16}H_{15}O_2NCl_2S$	54·0	4·4	53·9	4·2
m-O_2N·C_6H_4 [a]	42	240—242	$C_{16}H_{15}O_6N_3S$	51·2	4·3	50·9	4·0
3 : 4-CH_2O_2:C_6H_3	25	237—240	$C_{18}H_{17}O_6NS$	57·6	5·0	57·6	4·6

[a] Plates from acetone–ethanol. The hydrochlorides of the last two compounds did not crystallise. The *hydrochlorides* of the first four compounds had m. p. (all with decomp.) 275—278° (Found: Cl, 11·0. Reqd.: Cl, 11·0%), 268—270° (Found: Cl, 9·2. Reqd.: Cl, 9·2%), 245—247° (Found: Cl, 9·9. Reqd.: Cl, 10·1%), and 267—270° (Found: Cl, 9·2. Reqd.: Cl, 9·0%), respectively.

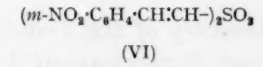
Unlike the esters, sulphonyldiacetic acid did not undergo this condensation in ethanol, but with several aldehydes and ammonium acetate in glacial acetic acid it gave, with decarboxylation, products of type (V) (for details see Table 3). These compounds form hydrochlorides which are stable in water and can be recrystallised from ethanol or



(IV)



(V)



(VI)

ethanol–ether. Sulphonyldiacetic acid with *m*-nitrobenzaldehehyde and ammonium acetate gives 2 : 2′-di-(*m*-nitrophenyl)divinyl sulphone (VI) in addition to the expected thiazine 1 : 1-dioxide.

EXPERIMENTAL

Diethyl Sulphonyldiacetate.—Sulphonyldiacetic acid (20 g.) (Alden and Houston, *J. Amer. Chem. Soc.*, 1934, **56**, 413) in absolute ethanol (100 c.c.) was saturated with dry hydrogen chloride. The excess of ethanol was removed by distillation and the residual solution was poured into water (150 c.c.). The separated liquid was taken up in ether and dried ($CaCl_2$); the solvent was removed and the residue distilled, giving the ester (24 g., 92%), b. p. 185—187°/10 mm. (cf. Backer, *loc. cit.*).

Dimethyl sulphonyldiacetate, similarly prepared in 96% yield, formed plates, m. p. 115—116° (from water) (Found: C, 34·6; H, 4·7. $C_6H_{10}O_6S$ requires C, 34·3; H, 4·8%).

Preparation of Substituted Tetrahydro-1 : 4-*thiazine* 1 : 1-*Dioxides from Sulphonyldiacetic Esters.*—The ester (0·01 mole), the aldehyde (0·02 mole), and ammonium acetate or the amine (0·01 mole) were refluxed in ethanol (20 c.c.) for 10—15 min. and then set aside overnight. The *compound* that separated was recrystallised from ethanol (see Tables 1 and 2).

Preparation of Substituted Tetrahydro-1 : 4-*thiazine* 1 : 1-*Dioxides from Sulphonyldiacetic*

Acid.—Sulphonyldiacetic acid (0·02 mole), the aldehyde (0·04 mole), and ammonium acetate (0·02 mole) were refluxed for 15—20 min. in glacial acetic acid (15 c.c.). After the evolution of carbon dioxide had subsided, the mixture was cooled and extracted with ether (30 c.c.). Dry hydrogen chloride was then passed through the ether solution which was set aside for a day. The *hydrochloride* that separated was recrystallised from ethanol or ethanol–ether. The *base* was liberated by dissolving the hydrochloride in ethanol, adding aqueous ammonia, and diluting with water (see Table 3).

Diethyl αα′-Dicinnamylidenesulphonyldiacetate [*Di-(1-ethoxycarbonyl-4-phenylbuta-1 : 3-dienyl) Sulphone*].—To an ethanolic solution of diethyl sulphonyldiacetate (2 g.), freshly distilled cinnamaldehyde (2·05 g.) and ammonium acetate (0·65 g.) were added and the mixture was refluxed for 10 min. Overnight, diethyl αα′-dicinnamylidenesulphonyldiacetate (2·5 g.) separated. Recrystallisation from ethanol gave yellow plates, m. p. 140—141° (Found: C, 67·0; H, 5·4; S, 7·1. Calc. for $C_{26}H_{26}O_6S$: C, 66·9; H, 5·6; S, 6·9%). Backer (*loc. cit.*) gives m. p. 134—136°.

Ethyl Coumarin-3-sulphonylacetate.—Diethyl sulphonyldiacetate (3 g.), salicylaldehyde (3·08 g.), and ammonium acetate (0·97 g.) gave this *compound* (2 g.) as plates, m. p. 195—196° (from ethanol) (Found: C, 53·0; H, 4·2; S, 10·75. $C_{13}H_{12}O_6S$ requires C, 52·7; H, 4·10; S, 10·8%).

Di-3-coumarinyl Sulphone.—Dimethyl sulphonyldiacetate (2·1 g.), salicylaldehyde (2·44 g.), and ammonium acetate (0·77 g.) were refluxed in 95% ethanol (20 c.c.) for 15 min. and left aside. Gradually, *di-3-coumarinyl sulphone* (2·3 g.) separated as pale yellow needles, m. p. 322—324° (decomp.) (from dioxan) (Found: C, 60·9; H, 3·0; S, 9·1. $C_{18}H_{10}O_6S$ requires C, 61·0; H, 2·8; S, 9·0%).

Methyl Coumarin-3-sulphonylacetate.—Evaporation of the solvent from the mother-liquor of the above preparation and removal of the unchanged salicylaldehyde from the residue with sodium carbonate solution gave *methyl coumarin-3-sulphonylacetate* (0·5 g.). It crystallised as shining plates (from ethanol), m. p. 214—216° (Found: C, 51·3; H, 3·8. $C_{12}H_{10}O_6S$ requires C, 51·05; H, 3·6%).

2 : 2′-*Di*-m-*nitrophenyldivinyl Sulphone.*—Sulphonyldiacetic acid (2 g.), *m*-nitrobenzaldehyde (3·32 g.), and ammonium acetate (0·9 g.) were refluxed in glacial acetic acid (3 c.c.) for 30 min. After cooling, the product was shaken with ether (30 c.c.), and the ether-insoluble material was dissolved in acetone and precipitated by water. The unsaturated *sulphone* (1 g.) was obtained as light-yellow needles, m. p. 179—180° (from acetone–ethanol) (Found: C, 53·8; H, 3·7. $C_{16}H_{12}O_6N_2S$ requires C, 53·3; H, 3·4%).

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The Chemistry of the Triterpenes and Related Compounds. Part XXV. Some Stereochemical Problems concerning Polyporenic Acid C.*

By A. BOWERS, T. G. HALSALL, and (in part) G. C. SAYER.

[Reprint Order No. 5361.]

The $C_{(16)}$-hydroxyl group of polyporenic acid C is shown to have the α-configuration. The configuration at $C_{(20)}$ of polyporenic acid C is discussed and shown to be the same as that of eburicoic acid. The formation and chemistry of a number of derivatives of 20-*iso*eburicane are described.

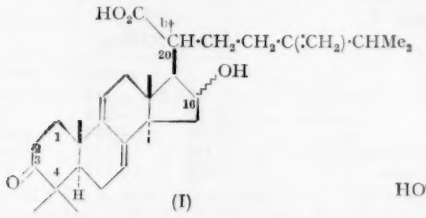
POLYPORENIC ACID C is a 16-hydroxy-derivative of 3-oxoeburico-7 : 9(11) : 24(28)-trien-21-oic acid (cf. I †) and it has been suggested that the hydroxyl group has the β-configuration (Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548). The only assumption made in arriving at this structure, apart from that concerning the configuration of the hydroxyl group, was that no stereochemical inversion occurred at $C_{(20)}$ during the conversion of polyporenic acid C into an eburicoic acid derivative. Biogenetic evidence supports this

* Part XXIV, *J.*, 1954, 2385.

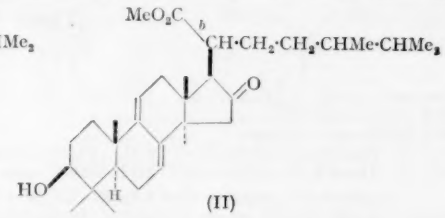
† The placing of a letter "b" against a bond attached to $C_{(20)}$ indicates that the substituent attached by the bond to $C_{(20)}$ is in the same relative configuration to $C_{(13)}$ as is the $C_{(21)}$-methyl group of lanostane. The placing of a letter "a" against a bond attached to $C_{(20)}$ indicates that the substituent attached by the bond to $C_{(20)}$ is in the same relative configuration to $C_{(13)}$ as is $C_{(22)}$ of lanostane.

assumption. Its chemical validity, and also the configuration of the hydroxyl group, are now discussed.

Reduction of the 3β-hydroxy-16-oxo-derivative (II) (Bowers *et al.*, *loc. cit.*) with lithium aluminium hydride gave two triols in approximately equal amounts. These must differ

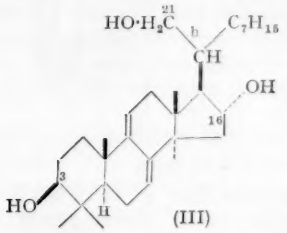


(I)

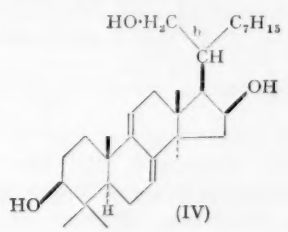


(II)

at $C_{(16)}$, one being the 3β : 16α : 21- and the other the corresponding 3β : 16β : 21-derivative (cf. III and IV). One of the triols was identical with that obtained by reduction of methyl dihydropolyporenate C successively with sodium borohydride and lithium aluminium hydride and hence must have the same configuration at $C_{(16)}$ as polyporenic acid C. This triol had a molecular rotation $[M]_D$ in pyridine of +179° whilst the other triol had $[M_D]$ +429°. Fukushima and Gallagher (*J. Amer. Chem. Soc.*, 1951, **73**, 196) have calculated molecular-rotation differences between 16α- and 16β-hydroxy-steroids and the corresponding deoxy-compounds. They found for the 16α-OH group $\Delta[M_D] = -44°$ to −77° and for the 16β-OH group $\Delta[M_D] = +33°$ to +40°. Hence $[M_D]$ 16β-OH minus $[M_D]$ 16α-OH is +77° to +111°, with the 16β-hydroxy-steroids more dextrorotatory (cf. Klyne and Stokes, *J.*, 1954, 1979). By analogy, therefore, the more dextrorotatory triol described above should be (IV), and the other, which is also obtained from methyl dihydropolyporenate C, should be the 3β : 16α : 21-triol (III). The molecular-rotation



(III)



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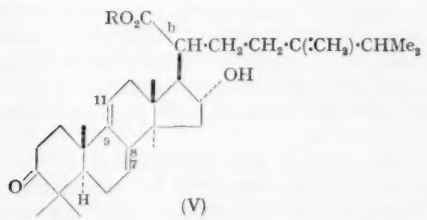


(V)

difference ($\Delta[M_D]$ 250°) between the triols is greater than that found for the steroids, but this is probably due to a vicinal effect between the oxygen functions at $C_{(16)}$ and $C_{(21)}$. This interpretation of the data leads to the α-configuration for the hydroxyl group of methyl dihydropolyporenate C and to structure (V) for polyporenic acid C. This conclusion is opposite to that previously suggested.

Acetylation of 16α-hydroxy-steroids results in a large negative shift in the molecular rotation while 16β-hydroxy-steroids give a positive shift (cf. Fukushima and Gallagher, *loc. cit.*; Klyne and Stokes, *loc. cit.*). Inspection of Table 1 shows that acetylation of the $C_{(16)}$ hydroxyl group of polyporenic acid C and its derivatives is accompanied by a large

negative shift in the molecular rotation, confirming the assignment of the α-configuration to this group.

The formation of two epimeric 16-hydroxy-derivatives on reduction of the 16-oxo-derivative (II) with lithium aluminium hydride is in contrast to the almost exclusive

TABLE 1.

	$[M_D]$ ($CHCl_3$)		
		Acetate	$\Delta Ac(C_{(16)})$
Polyporenic acid C	(+ 29°)†	−114°	[−143°]
Methyl polyporenate C	+ 49	−156	−205
Methyl dihydropolyporenate C	+ 50	−130	−180
Methyl 3β : 16α-dihydroxyeburico-7 : 9(11) : 24(28)-trien-21-oate	+138	+143	−150
Methyl 3β : 16α-dihydroxyeburico-7 : 9(11)-dien-21-oate	+136	+117	−174 *

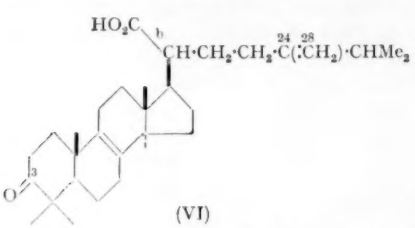
* Calculated by assuming that $\Delta Ac(3\beta\text{-OH})$ is +155°. This value is the mean of the ΔAc values quoted for the 3β-OH group of methyl dehydroeburicoate and methyl dehydrodihydroeburicoate (Gascoigne, Robertson, and Simes, *J.*, 1953, 1833). The ΔAc (3β-OH) for methyl 16β-chloro-3β-hydroxyeburico-7 : 9(11)-dien-21-oate (Bowers *et al.*, *loc. cit.*) is +171°. If this value is used instead of +155° then the $\Delta Ac(C_{(16)})$ values for the last two compounds become −166° and −190°.

† Measurements in pyridine solution. Ref.: Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548.

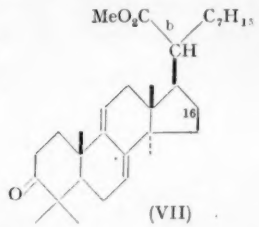
formation of the 16β-alcohol from 16-oxo-steroids (Hirshmann, *J. Biol. Chem.*, 1949, **178**, 751).

To study further the properties of the $C_{(16)}$ hydroxyl group of polyporenic acid C derivatives the carbonyl group of methyl dihydropolyporenate C was reduced by the Wolff–Kishner method.

Only one product was expected since similar reduction of eburiconic acid (VI) (Gascoigne, Holker, Ralph, and Robertson, *J.*, 1951, 2346), methyl 3β-acetoxy-16-oxoeburico-7 : 9(11)-dien-21-oate (Bowers *et al.*, *loc. cit.*), and methyl 24-oxo-28-noreburico-8-en-21-oate



(VI)



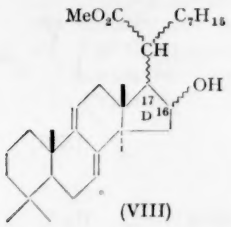
(VII)

(Holker, Powell, Robertson, Simes, Wright, and Gascoigne, *J.*, 1953, 2422) leads to only one reported product in each case. Further, reduction of (VII), differing from the dihydro-ester only in the absence of a hydroxyl group at $C_{(16)}$, followed by methylation of the product with diazomethane, gave only methyl eburico-7 : 9(11)-dien-21-oate. This was also formed, along with two nitrogenous compounds (see below), from the corresponding 3 : 16-dioxo-derivative. Compound (VII) was obtained by oxidation of the deacetylation product from methyl 3β-acetoxyeburico-7 : 9(11)-dien-21-oate prepared from polyporenic acid C as described by Bowers *et al.* (*loc. cit.*).

Reduction of the dihydro-ester and methylation of the product gave, however, two compounds which were readily separated by chromatography. Both were methyl monohydroxy-esters, $C_{32}H_{52}O_3$. For discussion they are designated "ester A" and "ester B," the yield of "B" being about twice that of "A." The most likely difference between them appeared to be in configuration at one or more of the carbon atoms 16, 17, and 20, owing to partial inversion brought about by alkali during the reduction (cf. VIII).

At first we were inclined to discount inversion at $C_{(20)}$, α to the ester group, in view of the absence of isomerisation in the reductions described above. The first possibility considered was epimerisation of the secondary alcohol group at $C_{(16)}$ during the reduction whilst a free 3-oxo-group was still present. The epimerisation of secondary alcohols by alkali at elevated temperatures in the presence of a ketone is well known (cf. Aschner and Doering, *J. Amer. Chem. Soc.*, 1949, **71**, 838). "Ester B" was heated with alkali and a small amount of fluorenone in ethylene glycol. The product was methylated and found to

be a mixture of " ester A " and " ester B " in the approximate ratio 1 : 2 similar to that found in the reduction. However, oxidation of the two esters with chromic acid gave *two* keto-esters. Hence " ester A " and " ester B " must either differ in configuration at $C_{(16)}$ and also at least one other carbon atom or have the same configuration at $C_{(16)}$ but



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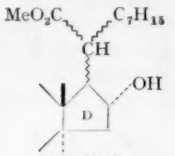
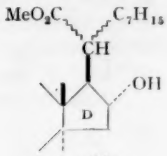


(IX)



(X)

differ elsewhere. The almost identical molecular-rotation differences found when the two hydroxy-esters are acetylated indicate that the second alternative is correct (cf. Table 2). The differences further indicate that the hydroxyl groups in both esters have the α-configuration (cf. IX).

A difference in configuration at $C_{(17)}$ was considered. A mechanism which would bring it about involves equilibration of the hydroxy-esters with small amounts of keto-esters in

TABLE 2.

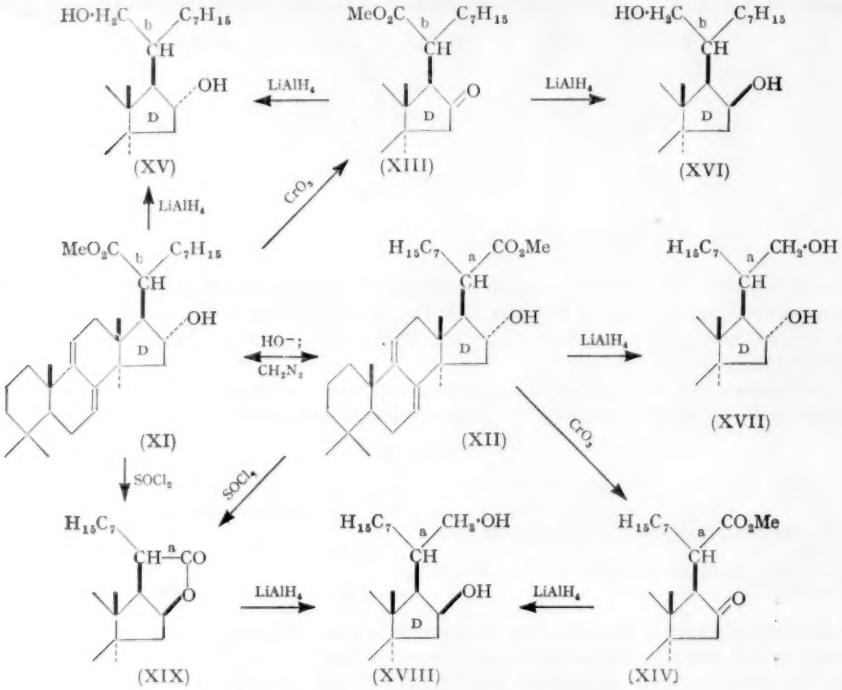
	$[M_D]$				
		Acetate	Ketone	ΔAc	ΔKet.
Methyl 16α-hydroxyeburico-7 : 9(11)-dien-21-oate (" ester A ")	+111°	−21°	−246°	−132°	−357°
Methyl 16α-hydroxy-20-*iso*eburico-7 : 9(11)-dien-21-oate (" ester B ")	+110	−37	−289	−147	−399

the reaction mixture. Isomerisation at a position α to a carbonyl group could then occur. In fact, as will become clear in the sequel, the side chains of both " ester A " and " ester B " must be *trans* to their respective 16-hydroxyl groups and hence both must have the β-configuration (cf. X). By exclusion therefore it is necessary to conclude that the esters differ at $C_{(20)}$.

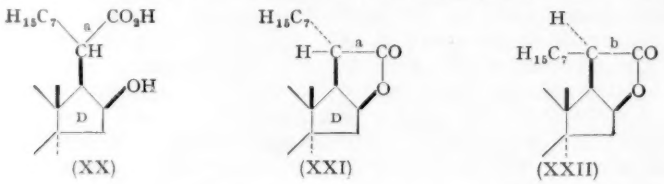
For simplification the chemistry of " ester A " and " ester B " is discussed in terms of their correct structures (XI; 20-normal series) and (XII; 20-*iso*-series) which follow from the arguments developed below. The ketone formed from " ester A " is (XIII; 20-normal series) and that from " ester B " is (XIV; 20-*iso*-series). Reduction of (XIII) with lithium aluminium hydride gave two diols (XV) and (XVI). One of these, (XV), was also obtained by direct reduction of " ester A " and must therefore be the 16α-hydroxy-derivative. (XVI) is then the 16β-hydroxy-derivative. Molecular rotations support these conclusions. The diol (XVI) has a higher molecular rotation ($[M_D]$ in pyridine = +470°) than the diol (XV) $[M_D]$ in pyridine = +205°), in agreement with the results quoted earlier for 16-hydroxy-steroids. On acetylation of (XV) a diacetate is obtained with $[M_D]$ in chloroform equal to +32°, *i.e.*, a large negative change had occurred. Lahey and Strasser (*J.*, 1951, 873) have found that monoacetylation of 3β : 21-dihydroxyeburico-8 : 24(28)-diene to the 21-monoacetate is accompanied by a small positive change in molecular rotation ($\Delta[M_D] = +29°$). Even allowing for a solvent effect it may be concluded that acetylation of the 16-hydroxyl group of (XV) is accompanied by a large negative change in molecular rotation, typical of that found with 16α-hydroxy-derivatives. Similar reduction of the ketone (XIV) from " ester B " gave only one diol (XVIII) which was different from that (XVII) obtained directly from " ester B." Thus (XVII) is the 16α-hydroxy- and (XVIII) the 16β-hydroxy-derivative. Again molecular rotations confirm this assignment. Diol (XVIII) has a higher positive rotation ($[M_D]$ in chloroform = +123°) than diol (XVII) ($[M_D]$ in chloroform = +45°), whilst acetylation of the 16α-diol (XVII) gives a diacetate with a negative rotation ($[M_D]$ in chloroform = −114°). The formation of two diols from the 16-oxo-derivative (XIII) of the 20-normal

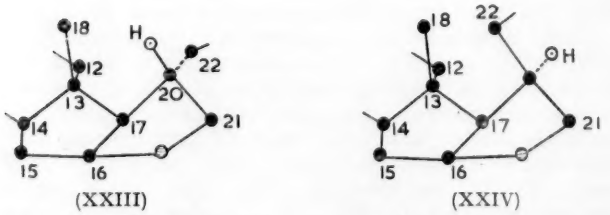
series corresponds to the formation of two triols from the corresponding 3β-hydroxy-16-oxo-derivative (II).

When the two hydroxy-esters (XI and XII) were treated with thionyl chloride in a



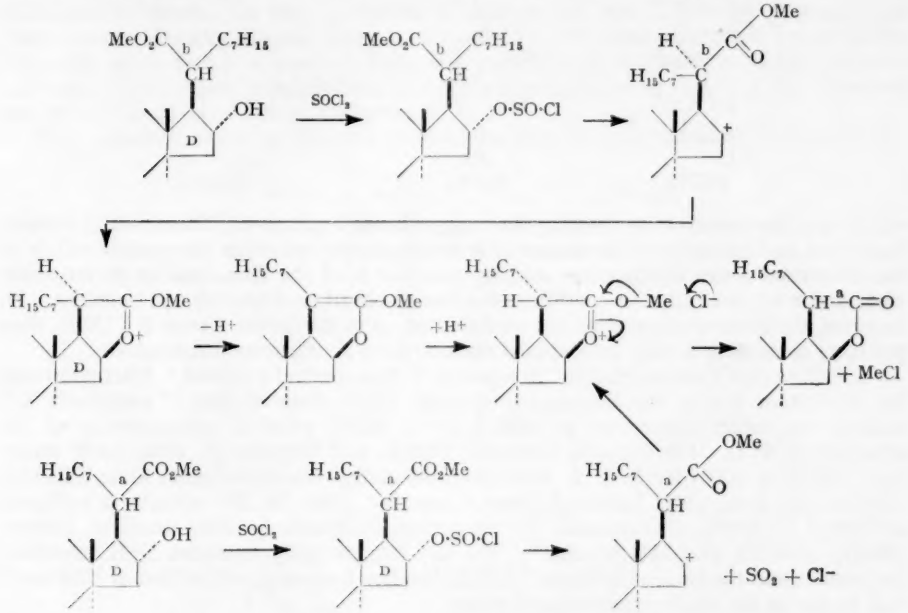
hydrocarbon solvent both yielded the *same* compound, $C_{31}H_{48}O_2$, the infra-red spectrum of which in carbon disulphide showed a band at 1771 cm.$^{-1}$ characteristic of a saturated γ-lactone. Reduction of the lactone with lithium aluminium hydride gave the diol (XVIII) obtained by similar reduction of the 16-oxo-derivative (XIV) from "ester B." The





lactone therefore must be derived from the hydroxy-acid (XX) which has the same configuration at $C_{(16)}$, $C_{(17)}$, and $C_{(20)}$ as the diol (XVIII). The 16-hydroxyl group of this diol has been shown above to have the β-configuration. On the

assumption that the lactone has a *cis*-structure the 17-side chain in both the lactone and the diol must also be β in configuration. There remains the problem of the configuration at $C_{(20)}$, the two possibilities in the case of the lactone being (XXI) and (XXII). Inspection of models indicates that the 20-*iso*-structure (XXI) (cf. XXIII *) should be much more stable than the 20-normal structure (XXII) (cf. XXIV *) since in the latter case there is very considerable compression between the 18-methyl group and the 22-methylene group. For this reason (XXI) is put forward for the lactone structure, with (XI) and (XII) following for " ester A " and " ester B " respectively. The suggested mechanisms for the formation of (XXI) from both esters are indicated below.

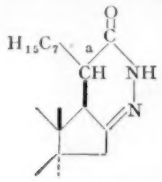


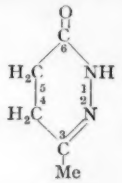
As indicated above, a number of Wolff–Kishner reductions have been carried out with eburicoic acid derivatives, *i.e.*, compounds without the 16-oxygen atom, without the formation of isomers. The reason for the formation of two products from the 16α-hydroxy-3-oxo-derivative (dihydro-V) is probably as follows. In the absence of a 16-hydroxyl group the normal configuration at $C_{(20)}$ is more stable than the *iso*-configuration. When a 16-hydroxyl group is present a 20-*iso*-ester may increase its stability by hydrogen-bond formation between the methoxycarbonyl and the hydroxyl group (cf. the formation of the 20-*iso*-lactone). The 20-normal ester is prevented from doing so, for hydrogen bonding can only occur in that conformation which leads to compression between the 22-methylene and 18-methyl groups (cf. XXIV). Hence it is possible for the energies of the 16α-hydroxy-ester of the 20-*normal* series, not stabilised by hydrogen bonding, and of the 16α-hydroxy-ester of the 20-*iso*-series, stabilised by hydrogen bonding, to become approximately equal. If this explanation is valid, the infra-red spectra of " ester A " and " ester B " should be significantly different. This is so. " Ester A " in Nujol shows only one band (at 3597 cm.$^{-1}$) due to the OH stretching frequency and one at 1713 cm.$^{-1}$ due to the carbonyl group of the ester grouping, whilst " ester B " in Nujol shows bands at 3356 (broad) and 3552 cm.$^{-1}$ (sharp) typical of a hydroxyl group involved in hydrogen bonding and a split band at 1724 and 1740 cm.$^{-1}$ due to a carbonyl group involved in hydrogen bonding.

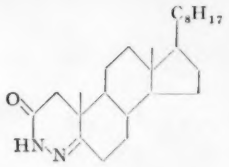
To study further the effect of alkali on the 20-position the ketones (XIII) from "ester A" and (XIV) from " ester B " were subjected to Wolff–Kishner reduction.

* These two figures are based on a drawing by Klyne (*Chem. and Ind.*, 1951, 426).

From (XIII), after methylation of the reduction product, the expected methyl eburico-7 : 9(11)-dien-21-oate was obtained. From (XIV) the *same* ester was obtained in *ca.* 10% yield, but the main product was a nitrogenous compound, $C_{31}H_{48}ON_2$. This was identical with " compound Y," one of two nitrogenous products obtained along with the above ester on reduction of methyl 3 : 16-dioxoeburico-7 : 9(11)-dien-21-oate. " Compound Y " is believed to be the tetrahydro-oxopyridazine derivative (XXV) derived by cyclisation of a 16-hydrazone grouping with the methoxycarbonyl group when in the 20-*iso*-configuration. Just as only this configuration favours lactone formation, so only it


(XXV)

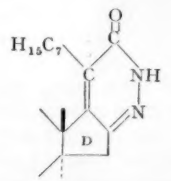

(XXVI)

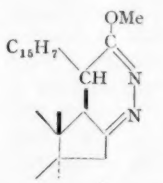

(XXVII)

will favour the formation of a tetrahydro-oxopyridazine derivative. These results indicate that when no 16-substituent is present after completion of reduction the product will be of the 20-normal series whether the starting material is of the 20-normal or 20-*iso*-series, since under vigorous alkaline conditions the less stable 20-*iso*-structure will isomerise. If, however, the 20-*iso*-configuration can be stabilised, as in the case of " ester B " (XII), then products containing it may be obtained starting from eburicoic acid derivatives.

Structure (XXV) is assigned to " compound Y " on spectral evidence. After allowance for absorption due to the conjugated eburico-7 : 9(11)-diene system, " compound Y " exhibits maximum absorption at 2430 Å (ε *ca.* 8000) which is characteristic of the grouping (XXVI). For instance, Overend, Turton, and Wiggins (*J.*, 1950, 3500) report $\lambda_{max.}$ 2430 Å (ε 6000) for 1 : 4 : 5 : 6-tetrahydro-3-methyl-6-oxopyridazine while (XXVII) (Weisenborn, Remy, and Jacobs, *J. Amer. Chem. Soc.*, 1954, **76**, 552) absorbs in methanol at 2440 Å (ε 8300). " Compound Y " in carbon disulphide exhibits bands at 1660(s), 1692(s), 3245(m), and 3441(m) cm.$^{-1}$. The last two probably represent N–H stretching frequencies and the band at 1660 cm.$^{-1}$ a N–H bending frequency, whilst that at 1692 cm.$^{-1}$ will be due to the amide-type carbonyl group.

When " compound Y " was treated with alkali a new compound (" compound Z ") was obtained. Its ultra-violet spectrum had a band at 2840 Å (ε 3600). A similar band is found with pyridazones (Overend *et al.*, *loc. cit.*) and it is likely that " compound Z " is the pyridazone (XXVIII), being formed by atmospheric oxidation during the alkaline treatment.


(XXVIII)

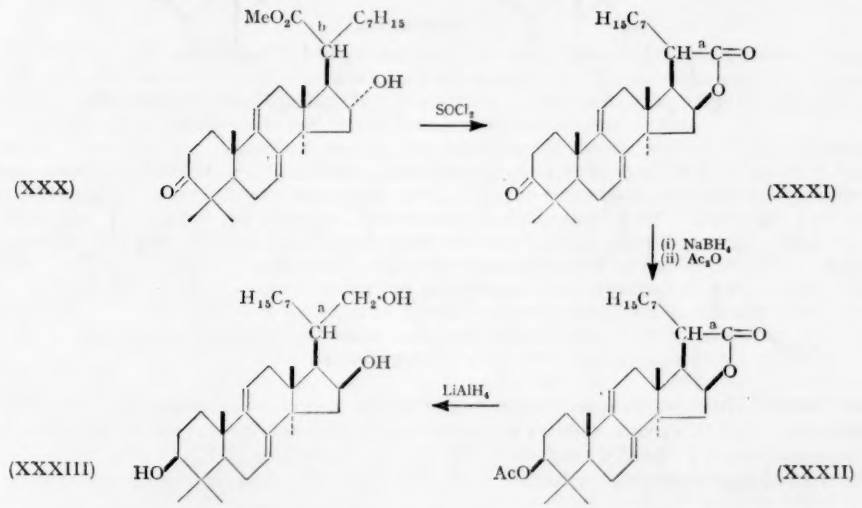

(XXIX)

Besides " compound Y " a second nitrogenous product (" compound X ") was obtained in small yield from methyl 3 : 16-dioxoeburico-7 : 9(11)-dien-21-oate. The main features of its infra-red spectrum determined in carbon disulphide [bands at 1618(s) and 3246(m) cm.$^{-1}$; shoulder at 1657 cm.$^{-1}$] are the presence of a band indicating either an OH or a >NH group, and the absence of a band corresponding to C=O stretching frequency. Its ultra-violet spectrum, in addition to showing very intense absorption in the region (2360—2520 Å) associated with the normal absorption of the eburico-7 : 9(11)-diene system, had an intense band at 3230—3300 Å (ε 19,300). At present it is not possible to put forward a satisfactory structure for " compound X." One possibility to be considered,

although it involves difficulties in the interpretation of the infra-red spectrum, is that it is a methylated product (*e.g.*, XXIX) formed during the diazomethane treatment after the completion of the reduction.

The results described above show that the isolation of deoxyeburicoic acid derivatives from Wolff–Kishner reductions does not necessarily prove that the carboxyl group in the starting material has the 20-normal configuration unless it is shown by other means that the configuration at $C_{(20)}$ in the reduction product is the same as in the starting material. In the inter-relation of eburicoic acid with lanosterol (Holker, Powell, Robertson, Simes, Wright, and Gascoigne (*loc. cit.*) specifically refer to this problem and provide the necessary additional evidence. In the conversion of polyporenic acid C into an eburicoic acid derivative (cf. Bowers, Halsall, Jones, and Lemin, *loc. cit.*) such evidence is not available. However, apart from that based on biogenetic arguments, it is possible to adduce chemical evidence to prove that in polyporenic acid C the configuration at $C_{(20)}$ is of the 20-normal and not of the 20-*iso*-eburicoic acid series.

The reduction of the 3β-hydroxy-16-oxo-derivative of polyporenic acid C (II) to the



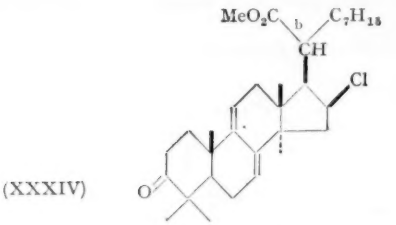
two triols, (III) and (IV), is analogous to the reduction of the ketone (XIII) from " ester A " by which two diols, (XV) and (XVI) are obtained, but not to that of the ketone (XIV) from " ester B " by which only one diol is obtained. This suggests that polyporenic acid C has the same configuration at $C_{(20)}$ as the ketone (XIII) from " ester A " of the 20-normal series.

If the 20-*iso*-structure were present in polyporenic acid C hydrogen bonding would occur in methyl polyporenate C between the methoxycarbonyl and the 16-hydroxyl group, as in the case of the analogous 20-*iso*-compound " ester B " (XII). The infra-red spectrum of methyl polyporenate C, however, indicates that no such hydrogen bonding occurs.

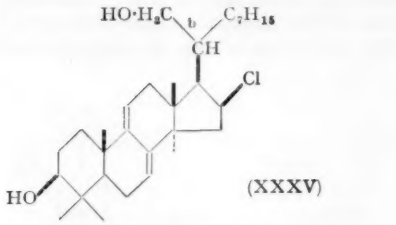
Treatment of methyl dihydropolyporenate C (XXX) with thionyl chloride in *iso*octane gave a lactone which, by analogy with the lactone (XXI) formed from both " ester A " and " ester B," must be the lactone (XXXI) of 16β-hydroxy-3-oxo-20-*iso*eburico-7 : 9(11)-dien-21-oic acid. Reduction of this lactone with sodium borohydride, followed by acetylation, gave the corresponding 3β-acetoxy-lactone (XXXII). This was in turn reduced with lithium aluminium hydride to a triol which must be 3β : 16β : 21-trihydroxy-20-*iso*-eburico-7 : 9(11)-diene (XXXIII). This triol was *not* identical with either of the triols, (III) and (IV), obtained by the lithium aluminium hydride reduction of the 3β-hydroxy-16-oxo-derivative (II) of methyl dihydropolyporenate C. One of these triols must have both its 3- and its 16-hydroxyl group in the β-configuration and hence must differ at $C_{(20)}$ from the triol from the lactone. Since the latter has the 20-*iso*-configuration the triol from

methyl dihydropolyporenate C, and hence polyporenic acid C, must have the 20-normal configuration and belong to the eburicoic acid series.

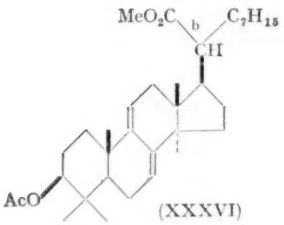
The tentative assignment of the β-configuration to the 16-hydroxyl group of polyporenic acid C by Bowers, Halsall, Jones, and Lemin (*loc. cit.*) was based on the interpretation of a most unexpected reaction of lithium aluminium hydride with the chloro-compound obtained by the action of phosphorus pentachloride on methyl dihydropolyporenate C. From this reduction, besides the expected chloro-diol, there was isolated the triol (III) obtained by the direct reduction of methyl dihydropolyporenate C with lithium aluminium hydride. On the assumption that the phosphorus pentachloride reaction brings about a S_N2 replacement of the 16-hydroxyl group by chlorine the chloro-ester obtained must be (XXXIV) and the chloro-diol (XXXV). Evidence that no drastic rearrangement had



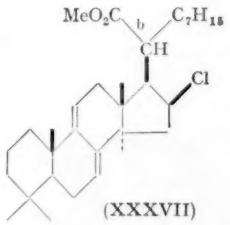
(XXXIV)



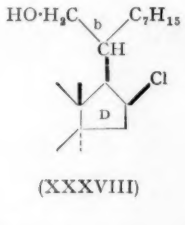
(XXXV)



(XXXVI)

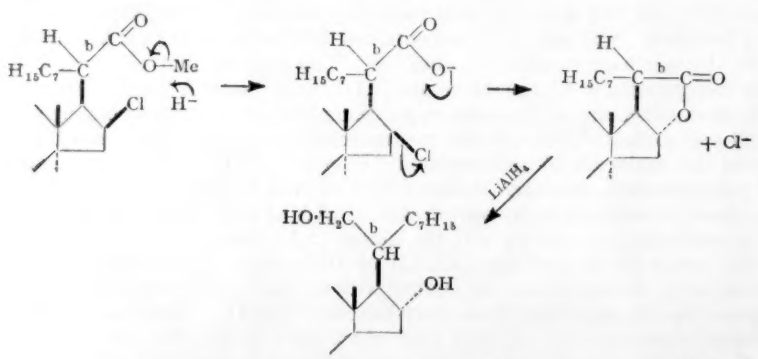


(XXXVII)



(XXXVIII)

been brought about by the phosphorus pentachloride was obtained when reduction of the chloro-ester (XXXIV) with sodium and *iso*propanol followed by acetylation gave methyl 3β-acetoxyeburico-7 : 9(11)-dien-21-oate (XXXVI). Structure (XXXIV) for the chloro-ester implies that during the reduction to the triol (III) the chlorine atom is replaced by a



hydroxyl group with *inversion* of configuration. A further example of this unusual reaction has also been provided in the 3-deoxy-series. Phosphorus pentachloride converted methyl 16α-hydroxyeburico-7 : 9(11)-dien-21-oate into a chloro-ester (XXXVII), reduction of which with lithium aluminium hydride led to a mixture of the chloro-alcohol (XXXVIII)

and the 16α : 21-dihydroxy-derivative (as XV). Again a chlorine atom has been replaced by a hydroxyl group with inversion of configuration.

The mechanism for this reaction which seems least unlikely is indicated below. The first step is O–alkyl fission of the ester grouping by hydride ion or its equivalent with the formation of the carboxylate anion. This then attacks $C_{(16)}$ from the rear-side, bringing about S_N2 displacement of chloride ion and the formation of a *trans*-γ-lactone. Inspection of models indicates that this is geometrically possible although the γ-lactone ring is strained. The lactone ring need only have transitory existence as it can be immediately attacked by lithium aluminium hydride with resultant fission to the 16α : 21-dihydroxy-derivative of the correct configuration. No evidence in support of this reaction mechanism has as yet been obtained. In its favour are that methyl polyporenate C is not easily hydrolysed and that alkaline hydrolysis of sterically hindered methyl esters may involve a S_N2-type displacement on the alkyl-carbon atom of the ester grouping accompanied by alkyl–oxygen fission rather than nucleophilic attack at the carbonyl-carbon atom (cf., for example, Goering, Rubin, and Newman, *J. Amer. Chem. Soc.*, 1954, **76**, 787).

Experimental

Rotations were determined in chloroform at room temperature unless otherwise stated. M. p.s were determined on a Kofler block and are corrected. The alumina used for chromatography had an activity I—II unless otherwise stated. Light petroleum refers to the fraction with b. p. 60—80°. Ultra-violet light absorption was determined in ethanol.

Note: The 16α- and 16β-indices used in the experimental section of Part XVIII (Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548) should be reversed in view of the proof given in this paper that the hydroxyl group of polyporenic acid C has the 16α- and not the 16β-configuration.

Reduction of Methyl 3β-Hydroxy-16-oxoeburico-7 : 9(11)-dien-21-oate (II) *with Lithium Aluminium Hydride.*—Methyl 3β-hydroxy-16-oxoeburico-7 : 9(11)-dien-21-oate (II) (535 mg.) in ether (150 c.c.) was treated with lithium aluminium hydride (500 mg.) at 20° for 24 hr. After destruction of the excess of reagent with ethyl acetate and decomposition of the complex with hydrochloric acid (2N; 100 c.c.) isolation with ether gave a product which was adsorbed from benzene (150 c.c.) on alumina (60 g.) which had been deactivated by being shaken in benzene with water (3 c.c.). Elution with benzene–ether (7 : 3; 500 c.c.) gave *eburico-7 : 9(11)-diene-3β : 16β : 21-triol* (IV) (300 mg.) as needles, m. p. 238—240° (after purification by chromatography and several crystallisations from methanol) depressed on admixture with 3β : 16α : 21-triol, $[\alpha]_D$ +91° (*c*, 0·88 in pyridine) (Found: C, 75·9; H, 11·05. $C_{31}H_{52}O_3,CH_3{\cdot}OH$ requires C, 76·1; H, 11·2%). Light absorption: Max., 2370, 2440, and 2520 Å, ε = 15,300, 18,000, and 11,900. Further elution with benzene–ether (1 : 1; 400 c.c.) gave eburico-7 : 9(11)-diene-3β : 16α : 21-triol (III) (200 mg.) as plates (from ethyl acetate), m. p. 234—235°, raised by several crystallisations from ethanol to 240—242°, undepressed on admixture with a specimen prepared from methyl dihydropolyporenate C, $[\alpha]_D$ +38° (*c*, 0·84 in pyridine).

Methyl 3-Oxoburico-7 : 9(11)-dien-21-oate (VII).—Methyl 3β-acetoxyeburico-7 : 9(11)-dien-21-oate (Part XVIII, *loc. cit.*) (500 mg.) was hydrolysed with methanolic potassium hydroxide (200 c.c.; 0·5%) for 24 hr. at 20°. After addition of water, extraction with ether yielded a product which was dissolved in acetone (75 c.c.) and oxidised with chromic acid in the usual manner (cf. Bowers *et al.*, *loc. cit.*). Isolation with ether gave a product which was adsorbed from light petroleum (50 c.c.) on alumina (30 g.). Elution with light petroleum–benzene (1 : 1; 600 c.c.) afforded methyl 3-oxoeburico-7 : 9(11)-dien-21-oate as needles, m. p. 156—158° (after several crystallisations from methanol), $[\alpha]_D$ +24° (*c*, 1·1) (Found: C, 79·85; H, 10·5. Calc. for $C_{32}H_{50}O_3$: C, 79·6; H, 10·45%) [Gascoigne, Robertson, and Simes (*J.*, 1953, 1835) give m. p. 155—155·5°, $[\alpha]_D$ +24°, for methyl 3-oxoeburico-7 : 9(11)-dien-21-oate]. Light absorption: Max., 2360, 2430, and 2510 Å, ε = 16,200, 18,600, and 8750.

Methyl Eburico-7 : 9(11)-dien-21-oate.—Methyl 3-oxoeburico-7 : 9(11)-dien-21-oate (VII) (80 mg.) in ethylene glycol (30 c.c.) was heated with hydrazine hydrate (1 c.c.; 60%) at 100° for 40 min. Potassium hydroxide (175 mg.) was then added and the solution heated under reflux for 5 hr. After acidication with acetic acid and dilution with water, extraction with ether yielded a product which was suspended in acetone (15 c.c.) and treated with ethereal diazomethane for 16 hr. at 20°. The methylated product was adsorbed from pentane (10 c.c.) on alumina (10 g.). Elution with light petroleum (300 c.c.) gave *methyl eburico-7 : 9(11)-dien-21-oate* (62 mg.) as plates, m. p. 137—139° (several crystallisations from methanol), $[\alpha]_D$ +36°

(*c*, 0·79) (Found: C, 81·5; H, 11·2. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). Light absorption: Max., 2370, 2440, and 2520 Å, ε = 14,950, 17,550, and 11,350.

Wolff–Kishner Reduction of Methyl 16α-*Hydroxy*-3-*oxoeburico*-7 : 9(11)-*dien*-21-*oate*.—Methyl 16α-hydroxy-3-oxoeburico-7 : 9(11)-dien-21-oate (2·4 g.) in diethylene glycol (120 c.c.) was heated at 100° for 1 hr. with hydrazine hydrate (5 c.c.; 90%), after which the excess of hydrazine and water was removed by distillation. Potassium hydroxide (2·0 g.) was then added and the solution heated under reflux for 5 hr. After acidification with acetic acid and dilution with water, ether-extraction yielded a product which was suspended in acetone and treated with an excess of ethereal diazomethane at 20° for 16 hr. The resulting mixture of methyl esters was adsorbed from benzene on alumina (150 g.). Elution with benzene–ether (7 : 1; 2 l.) gave *methyl* 16α-*hydroxyeburico*-7 : 9(11)-*dien*-21-*oate* ("ester A") (XI) (0·80 g.) as needles, m. p. 184—185° (after several crystallisations from methanol), $[\alpha]_D$ +23° (*c*, 0·81) (Found: C, 79·3; H, 10·8. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). Light absorption: Max., 2370, 2440, and 2520 Å, ε = 15,500, 18,200, and 12,050. Infra-red absorption in Nujol: bands at 1713 and 3597 cm.$^{-1}$.

Further elution with benzene–ether (1 : 1; 2·5 l.) gave *methyl* 16α-*hydroxy*-20-iso-*eburico*-7 : 9(11)-*dien*-21-*oate* ("ester B") (XII) (1·5 g.) as needles, m. p. 146—148° (after purification by chromatography and several crystallisations from methanol), $[\alpha]_D$ +22° (*c*, 0·90) (Found: C, 78·0; H, 10·7. $C_{32}H_{52}O_3,\frac{1}{2}CH_3{\cdot}OH$ requires C, 77·95; H, 10·85%). Light absorption: Max., 2360, 2440, and 2520 Å; ε = 14,300, 16,700, and 11,000. Infra-red absorption in Nujol: bands at 1724, 1740, 3356 (broad), and 3552 (sharp) cm.$^{-1}$.

Partial Isomerisation of Methyl 16α-*Hydroxy*-20-iso-*eburico*-7 : 9(11)-*dien*-21-*oate to Methyl* 16α-*Hydroxyeburico*-7 : 9(11)-*dien*-21-*oate with Alkali*.—Methyl 16α-hydroxy-20-*iso*eburico-7 : 9(11)-dien-21-oate (525 mg.) in diethylene glycol (50 c.c.) was heated under reflux. With potassium hydroxide (500 mg.) and fluorenone (15 mg.) for 3½ hr. After acidification with acetic acid and dilution with water the product was separated by filtration and dried. It was suspended in acetone (50 c.c.) and methylated with ethereal diazomethane at 20° for 16 hr. The methylated product was adsorbed from benzene (50 c.c.) on alumina (50 g.). Elution with benzene–ether (4 : 1; 400 c.c.) gave methyl 16α-hydroxyeburico-7 : 9(11)-dien-21-oate (135 mg.) as needles, m. p. 180—182° (after several crystallisations from methanol), undepressed on admixture with an authentic sample, $[\alpha]_D$ +25° (*c*, +0·94).

Elution with benzene–ether (1 : 1; 400 c.c.) gave methyl 16α-hydroxy-20-*iso*-eburico-7 : 9(11)-dien-21-oate (310 mg.) as needles (from methanol–nitromethane), m. p. 143—145° (after several crystallisations from methanol–nitromethane), undepressed on admixture with an authentic sample, $[\alpha]_D$ +24°, (*c*, 1·16).

Methyl 16α-*Acetoxyeburico*-7 : 9(11)-*dien*-21-*oate*.—Methyl 16α-hydroxyeburico-7 : 9(11)-dien-21-oate (200 mg.) in pyridine (10 c.c.), treated with acetic anhydride (1 c.c.) at 20° for 24 hr., gave a product which was adsorbed from light petroleum (100 c.c.) on alumina (30 g.). Elution with light petroleum–benzene (1 : 1; 250 c.c.) gave the 16α-*acetoxy-ester* as needles, (190 mg.), m. p. 123—125° (after several crystallisations from methanol), $[\alpha]_D$ −4° (*c*, 1·06) (Found: C, 76·9; H, 10·85. $C_{34}H_{54}O_4$ requires C, 77·5; H, 10·35%). Light absorption: Max., 2360, 2430, and 2510 Å, ε = 13,350, 16,900, and 10,000.

Methyl 16α-*Acetoxy*-20-iso-*eburico*-7 : 9(11)-*dien*-21-*oate*.—Methyl 16α-hydroxy-20-*iso*-eburico-7 : 9(11)-dien-21-oate (500 mg.) in pyridine (20 c.c.), treated with acetic anhydride (2·5 c.c.) at 20° for 24 hr., gave the 16α-*acetoxy-ester* as a white solid (480 mg.) which was crystallised several times from methanol–ethyl acetate, giving needles, m. p. 178—180°, $[\alpha]_D$ −7° (*c*, 1·0) (Found: C, 77·55; H, 10·45. $C_{34}H_{54}O_4$ requires C, 77·5; H, 10·35%). Light absorption: Max., 2360, 2430, and 2510 Å, ε = 14,050, 16,350, and 10,860.

Methyl 16-*Oxoeburico*-7 : 9(11)-*dien*-21-*oate* (XIII).—Methyl 16α-hydroxyeburico-7 : 9(11)-dien-21-oate (110 mg.) in acetone (25 c.c.) was oxidised with chromic acid in the usual manner (cf. Bowers *et al.*, *loc. cit.*). Isolation with ether gave a product which was adsorbed from benzene (5 c.c.) on alumina (6 g.). Elution with benzene (150 c.c.) gave *methyl* 16-*oxoeburico*-7 : 9(11)-*dien*-21-*oate* (85 mg.) as plates, m. p. 159·5—161° (after several crystallisations from methanol), $[\alpha]_D$ −51° (*c*, 0·98) (Found: C, 79·85; H, 10·5. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). Light absorption: Max., 2430 Å; ε = 17,600; inflexions, 2360 and 2510 Å, ε = 15,600 and 11,900.

Methyl 16-*Oxo*-20-iso*eburico*-7 : 9(11)-*dien*-21-*oate* (XIV).—Methyl 16α-hydroxy-20-*iso*eburico-7 : 9(11)-dien-21-oate (290 mg.) in acetone (25 c.c.) was oxidised with chromic acid in the usual manner. Isolation with ether gave a product which was absorbed from light petroleum on alumina (25 g.). Elution with benzene gave *methyl* 16-*oxo*-20-iso*eburico*-7 : 9(11)-*dien*-

21-*oate* (220 mg.) as needles, m. p. 120—121° (after several crystallisations from methanol), $[\alpha]_D$ −60° (*c*, 1·07) (Found: C, 79·75; H, 10·45. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). Light absorption: Max., 2430 Å, ε = 18,400; inflexions, 2370 and 2510 Å, ε = 16,300 and 12,200.

Eburico-7 : 9(11)-*diene*-16α : 21-*diol* (XV).—Methyl 16α-hydroxyeburico-7 : 9(11)-dien-21-oate (XI) (600 mg.) in ether (150 c.c.) was heated under reflux with lithium aluminium hydride (400 mg.) for 45 min. The excess of reagent was destroyed with ethyl acetate, and the complex decomposed with hydrochloric acid (2N; 100 c.c.). Isolation with ether gave the 16α : 21-*diol* (XV) (530 mg.) as needles, m. p. 247—249° (after several crystallisations from ethanol), $[\alpha]_D$ +45° (*c*, 0·95 in pyridine) (Found: C, 81·4; H, 11·6. $C_{31}H_{52}O_2$ requires C, 81·5; H, 11·5%). Light absorption: Max., 2360 and 2440 Å, ε = 14,400, and 17,000; inflexion, 2510 Å, ε = 11,100.

This diol (170 mg.) in pyridine (15 c.c.), treated with acetic anhydride (2·5 c.c.) at 20° for 15 hr., gave a product which was adsorbed from benzene (15 c.c.), on alumina (15 g.). Elution with light petroleum–benzene (1 : 1; 600 c.c.) gave 16α : 21-*diacetoxyeburico*-7 : 9(11)-*diene* (120 mg.) as needles, m. p. 135—136° (after several crystallisations from methanol), $[\alpha]_D$ +6° (*c*, 0·98) (Found: C, 78·0; H, 10·3. $C_{35}H_{56}O_4$ requires C, 77·75; H, 10·45%). Light absorption: Max., 2360, 2430, and 2510 Å, ε = 15,700, 18,200, and 11,900.

Reduction of Methyl 16-*Oxoeburico*-7 : 9(11)-*dien*-21-*oate* (XIII) *with Lithium Aluminium Hydride*.—The ester (350 mg.) in ether (100 c.c.) was treated with lithium aluminium hydride (350 mg.) at 20° for 16 hr. Isolation as above yielded a product which was absorbed from benzene (30 c.c.) on alumina (40 g.). Elution with benzene–ether (4 : 1; 500 c.c.) gave *eburico*-7 : 9(11)-*diene*-16β : 21-*diol* (XVI) (150 mg.) as needles, m. p. 247—249° (after several crystallisations from ethanol) (depressed on admixture with the 16α : 21-diol), $[\alpha]_D$ +103° (*c*, 1·2 in pyridine) (Found: C, 81·15; H, 11·6%). Light absorption: Max. 2360, 2440, and 2520 Å, ε = 14,050, 16,700, and 11,500.

Elution with benzene–ether (7·3; 500 c.c.) gave the 16α : 21-diol (135 mg.), m. p. 246—248° (after several crystallisations from ethanol; undepressed on admixture with an authentic sample), $[\alpha]_D$ +43° (*c*, 0·91 in pyridine).

Reduction of Methyl 16α-*Hydroxy*-20-iso*eburico*-7 : 9(11)-*dien*-21-*oate with Lithium Aluminium Hydride*.—Methyl 16α-hydroxy-20-*iso*eburico-7 : 9(11)-dien-21-oate (XII) (230 mg.) in ether (75 c.c.) was heated under reflux with lithium aluminium hydride (200 mg.) for 1 hr. The product was isolated and chromatographed as above on alumina (20 g.). Elution with benzene–ether (7 : 3; 500 c.c.) gave 20-iso*eburico*-7 : 9(11)-*diene*-16α : 21-*diol* (XVII) (180 mg.) as needles, m. p. 189—191° (after several crystallisations from methanol), $[\alpha]_D$ +10° (*c*, 1·09) (Found: C, 81·7; H, 11·4%). Light absorption: Max., 2360, 2430, and 2520 Å, ε = 13,200, 15,300, and 10,300.

Acetylation, as above, of the diol (350 mg.) for 24 hr. gave a product which was adsorbed from light petroleum (30 c.c.) on alumina (45 g.). Elution with benzene (500 c.c.) gave 16α : 21-*diacetoxy*-20-iso*eburico*-7 : 9(11)-*diene* (310 mg.) as needles, m. p. 109—111° (after several crystallisations from methanol), $[\alpha]_D$ −21° (*c*, 0·93) (Found: C, 78·05; H, 10·5%). Light absorption in ethanol: Max., 2360, 2430, and 2510 Å, ε = 14,600, 16.900, and 11,300. Further elution with ether (300 c.c.) gave a small amount of unchanged starting material.

Reduction of Methyl 16-*Oxo*-20-iso*eburico*-7 : 9(11)-*dien*-21-*oate with Lithium Aluminium Hydride*.—The keto-ester (XIV) (205 mg.) in ether (100 c.c.) was treated with lithium aluminium hydride at 20° for 16 hr. Isolation as above gave a product which was adsorbed from benzene (20 c.c.) on alumina (20 g.). Elution with benzene–ether (1 : 1; 300 c.c.) gave 20-*iso*eburico-7 : 9(11)-diene-16β : 21-diol (175 mg.) as needles, m. p. 214—215° (after several crystallisations from ethanol–nitromethane), undepressed on admixture with a specimen prepared by the reductive fission of the lactone of 16β-hydroxy-20-*iso*eburico-7 : 9(11)-dien-21-oic acid (see below), $[\alpha]_D$ +27° (*c*, 0·93).

Reaction of Methyl 16α-*Hydroxyeburico*-7 : 9(11)-*dien*-21-*oate* (XI) *with Thionyl Chloride*.—Methyl 16α-hydroxyeburico-7 : 9(11)-dien-21-oate (265 mg.) in light petroleum (b. p. 80—100°) was heated under reflux with thionyl chloride (0·25 c.c.) for 2 hr. After addition of water, isolation with light petroleum yielded a product which was adsorbed from light petroleum (30 c.c.) on alumina (30 g.). Elution with light petroleum–benzene (7 : 3; 400 c.c.) gave the *lactone* (XIX) (73 mg.) of 16β-hydroxy-20-*iso*eburico-7 : 9(11)-dien-21-oic acid as needles, m. p. 202—204° (after several crystallisations from methanol), $[\alpha]_D$ −13° (*c*, 1·12) (Found: C, 82·25; H, 10·9. $C_{31}H_{48}O_2$ requires C, 82·2; H, 10·7%). Light absorption: Max., 2430 Å, ε = 16,000; inflexions, 2360 and 2510 Å, ε = 13,800 and 10,500. Infra-red absorption in CS_2: band at 1771 cm.$^{-1}$.

Reaction of Methyl 16α-*Hydroxy*-20-iso*eburico*-7 : 9(11)-*dien*-21-*oate* (XII) *with Thionyl Chloride*.—Methyl 16α-hydroxy-20-*iso*eburico-7 : 9(11)-dien-21-oate (290 mg.) in benzene (20 c.c.) was heated under reflux with thionyl chloride (0·35 c.c.) for 1 hr. After addition of water, isolation with benzene gave the lactone of 16β-hydroxy-20-*iso*eburico-7 : 9(11)-dien-21-oic acid as needles (220 mg.), m. p. 202—204° [three crystallisations from methanol; undepressed on admixture with the lactone obtained by the action of thionyl chloride on methyl 16α-hydroxy-eburico-7 : 9(11)-dien-21-oate], $[\alpha]_D$ −13° (*c*, 1·11). The infra-red spectra of the lactones from the two esters were identical.

Reduction of the Lactone (XIX) *with Lithium Aluminium Hydride*.—The lactone (185 mg.) in ether (100 c.c.) was heated under reflux with lithium aluminium hydride (200 mg.) for 1·5 hr. Isolation as usual yielded a product which was adsorbed from benzene on alumina (10 g.). Elution with benzene–ether (3 : 2; 300 c.c.) gave 20-iso*eburico*-7 : 9(11)-*diene*-16β : 21-*diol* (160 mg.) as needles, m. p. 214—215° (after several crystallisations from ethanol–nitromethane), $[\alpha]_D$ +27° (*c*, 1·15) (Found: C, 81·65; H, 11·6%). Light absorption: Max., 2360, 2440, and 2520 Å, ε = 13,300, 15,700, and 10,400. It gave on acetylation a gum, $[\alpha]_D$ +102° (*c*, 1·01).

Wolff–Kishner Reduction of Methyl 3 : 16-*Dioxoeburico*-7 : 9(11)-*dien*-21-*oate*.—Methyl 3 : 16-dioxoeburico-7 : 9(11)-dien-21-oate (1·3 g.) was reduced under the conditions described above for the reduction of methyl 3-oxoeburico-7 : 9(11)-dien-21-oate. The methylated reduction product was adsorbed from light petroleum–benzene (4 : 1; 200 c.c.) on alumina (75 g.). Elution with light petroleum–benzene (4 : 1; 500 c.c.) gave methyl eburico-7 : 9(11)-dien-21-oate (300 mg.) as plates, m. p. 139—141° [after several crystallisations from methanol; undepressed on admixture with a sample prepared from methyl 3-oxoeburico-7 : 9(11)-dien-21-oate], $[\alpha]_D$ +40° (*c*, 0·95).

Elution with light petroleum–benzene (1 : 1; 400 c.c.) gave "*compound X*" (168 mg.) as needles, m. p. 210—213° (after purification by chromatography and several crystallisations from ethyl acetate), $[\alpha]_D$ −200° (*c*, 0·87) (Found: C, 80·1; H, 9·9. $C_{31}H_{48}ON_2$ requires C, 80·1; H, 10·4. $C_{31}H_{46}ON_2$ requires C, 80·45; H, 10·0. $C_{32}H_{50}ON_2$ requires C, 80·3; H, 10·5%. Light absorption: Max., 2370, 2430, and 3230—3300 Å, ε = 22,400, 23,200, and 19,350; inflexion, 2510 Å, ε = 17,800. Infra-red absorption in CS_2: bands at 1618(s), 1657(sh)(m), and 3246(m) cm.$^{-1}$.

Elution with benzene–ether (1 : 1; 600 c.c.) gave "*compound Y*" (XXV) (585 mg.) as needles, m. p. 224—226° (several crystallisations from ethyl acetate), $[\alpha]_D$ −124° (*c*, 1·03) (Found: C, 80·25; H, 10·1; N, 6·3. $C_{31}H_{48}ON_2$ requires C, 80·1; H, 10·4; N, 6·05%). Light absorption: Max., 2430 Å, ε = 22,400; inflexions, 2360 and 2510 Å, ε = 19,150 and 16,900. Infra-red absorption in CS_2: bands at 1660(s), 1692(s), 1744(vw), 3245(m), and 3441(m).

Action of Alkali on Compound Y (XXV).—Compound Y (270 mg.) in diethylene glycol (50 c.c.) containing potassium hydroxide (200 mg.) was heated under reflux for 1½ hr. After acidification with acetic acid the mixture was diluted with water. Isolation with ether yielded a product which was adsorbed on alumina (30 g.). Elution with benzene–ether (1 : 1; 300 c.c.) gave "compound Y" (165 mg.) as needles, m. p. 226—228° (from ethyl acetate; undepressed on admixture with starting material), $[\alpha]_D$ −128° (*c*, 0·92).

Elution with benzene–ether (3 : 7; 200 c.c.) gave "*compound Z*" (58 mg.) as needles, m. p. 281—284° (from ethyl acetate), $[\alpha]_D$ +50° (*c*, 0·78) (Found: C, 80·1; H, 10·1. $C_{31}H_{46}ON_2$ requires C, 80·45; H, 10·0%). Light absorption: Max., 2420 and 2840 Å, ε = 21,100, and 3600; inflexions, 2360 and 2510 Å, ε = 19,800 and 14,000. Infra-red absorption in CCl_4: bands at 1631(s), 1653(s), 1746(w), 3153(m), 3265(sh), and 3426(mw).

Wolff–Kishner Reduction of Methyl 16-*Oxoeburico*-7 : 9(11)-*dien*-21-*oate* (XIII).—Methyl 16-oxoeburico-7 : 9(11)-dien-21-oate (300 mg.) in diethylene glycol (50 c.c.) was heated at 100° 3 hr. with hydrazine hydrate (2 c.c.; 60%). Potassium hydroxide (0·3 g.) was added and the excess of water removed by distillation. The solution was then heated under reflux for 7 hr. After acidification with acetic acid and dilution with water, extraction with ether yielded a product which was suspended in acetone (70 c.c.) and treated with ethereal diazomethane at 20° for 24 hr. The methylated product was adsorbed from light petroleum on alumina (30 g.). Elution with light petroleum–benzene (9 : 1; 300 c.c.) gave methyl eburico-7 : 9(11)-dien-21-oate (70 mg.) as plates, m. p. and mixed m. p. 139—141° (after several crystallisations from methanol), $[\alpha]_D$ +42° (*c*, 0·99).

Wolff–Kishner Reduction of Methyl 16-*Oxo*-20-iso-*eburico*-7 : 9(11)-*dien*-21-*oate* (XIV).—The keto-ester (450 mg.) in diethylene glycol (50 c.c.) was heated at 100° for 2 hr. with hydrazine hydrate (3 c.c.; 60%). Potassium hydroxide (0·45 g.) was added and the excess of water

removed by distillation. The solution was heated under reflux for 5½ hr. After isolation and methylation as in the preceding case the product was adsorbed from light petroleum (200 c.c.) on alumina (45 g.). Elution with light petroleum–benzene (9 : 1; 200 c.c.) gave methyl eburico-7 : 9(11)-dien-21-oate (40 mg.) as needles, m. p. and mixed m. p. 137—139° (from methanol), $[\alpha]_D$ +42° (*c*, 0·96). Further elution with benzene–ether (1 : 1; 500 c.c.) afforded "compound Y" (XXV) (300 mg.) as needles, m. p. 222—224° (after several crystallisations from ethyl acetate), $[\alpha]_D$ −125° (*c*, 1·03). Its infra-red spectrum was identical with that of an authentic sample.

Reaction of Methyl 16α-*Hydroxy*-3-*oxoeburico*-7 : 9(11)-*dien*-21-*oate* (*Methyl Dihydropolyporenate C*) (XXX) *with Thionyl Chloride.*—Methyl dihydropolyporenate C (500 mg.) in *iso*-octane (50 c.c.) was heated with thionyl chloride (0·5 c.c.) at 100° for 2 hr. After addition of water, isolation with benzene gave a product which was adsorbed from light petroleum on alumina (50 g.). Elution with benzene (500 c.c.) gave the *lactone* (XXXI) (300 mg.) of 16β-hydroxy-3-oxo-20-*iso*-eburico-7 : 9(11)-dien-21-oic acid as needles, m. p. 247—249° (after several crystallisations from ethyl acetate and ethanol–chloroform), $[\alpha]_D$ −14° (*c*, 1·11) (Found: C, 79·5; H, 10·15. $C_{31}H_{46}O_3$ requires C, 79·8; H, 9·9%). Light absorption: Max., 2360, 2430, and 2500 Å, ε = 14,500, 16,600, and 10,950. Infra-red absorption in CCl_4: bands at 1713 and 1766 cm.$^{-1}$.

Lactone of 3β-*Acetoxy*-16β-*hydroxy*-20-iso*eburico*-7 : 9(11)-*dien*-21-*oic Acid* (XXXII).—The lactone of 16β-hydroxy-3-oxo-20-*iso*-eburico-7 : 9(11)-dien-21-oic acid (400 mg.) in dioxan (75 c.c.) was treated with sodium borohydride (100 mg.) in aqueous dioxan (1 : 1; 3 c.c.) at 20° for 1½ hr. After addition of water, isolation with ether yielded a product which was acetylated in pyridine (10 c.c.) with acetic anhydride (3 c.c.) at 100° for 1 hr. The acetylated product was isolated with ether and adsorbed from light petroleum (50 c.c.) on alumina (50 g.). Elution with benzene (400 c.c.) gave the *lactone* (310 mg.) of 3β-acetoxy-16β-hydroxy-20-*iso*-eburico-7 : 9(11)-dien-21-oic acid as needles (from methanol, m. p. 207—210°) (several crystallisations from light petroleum), $[\alpha]_D$ +29° (*c*, 1·3) (Found: C, 77·9; H, 10·15. $C_{33}H_{50}O_4$ requires C, 77·6; H, 9·9%). Light absorption: Max., 2360 and 2430 Å, ε = 15,600 and 18,100; inflexion, 2500 Å, ε = 11,750. Infra-red absorption in CCl_4: bands at 1733 and 1771 cm.$^{-1}$.

Reduction of the Lactone of 3β-*Acetoxy*-16β-*hydroxy*-20-iso-*eburico*-7 : 9(11)-*dien*-21-*oic Acid with Lithium Aluminium Hydride.*—The lactone (106 mg.) in ether (50 c.c.) was heated under reflux with lithium aluminium hydride (150 mg.) for 1·25 hr. Isolation as usual yielded a product (88 mg.) which was adsorbed from benzene (75 c.c.) on alumina (10 g.) which had been deactivated by shaking a suspension in benzene with water (0·5 c.c.). Elution with benzene–ether (3 : 1; 300 c.c.) gave 20-iso-*eburico*-7 : 9(11)-*diene*-3β : 16β : 21-*triol* (XXXIII) (71 mg.) as needles, m. p. 233—235° (after several crystallisations from ethyl acetate), depressed on admixture with the 3β : 16α : 21-trihydroxy-7 : 9(11)-diene, $[\alpha]_D$ +38° (*c*, 0·98) (Found: C, 78·4; H, 11·0. $C_{31}H_{52}O_3$ requires C, 78·75; H, 11·1%). Light absorption: Max., 2370, 2440, and 2520 Å, ε = 14,400, 16,800, and 11,550.

Reduction of Methyl 16β-*Chloro*-3-*oxoeburico*-7 : 9(11)-*dien*-21-*oate* (XXXIV) *with Sodium and* iso*Propyl Alcohol.*—Sodium (2·3 g.) was added to the chloro-ester (530 mg.) in *iso*propyl alcohol (50 c.c.), and the solution heated under reflux for 40 min. After dilution with water, isolation with ether gave a product which was acetylated in pyridine (10 c.c.) with acetic anhydride (5 c.c.) for 16 hr. at 20°. Isolation with ether yielded a product which was adsorbed from light petroleum (100 c.c.) on alumina (50 g.). Elution with benzene–ether (9 : 1; 400 c.c.) gave methyl 3β-acetoxyeburico-7 : 9(11)-dien-21-oate (440 mg.) as needles (from methanol), m. p. and mixed m. p. 172—174° (after several crystallisations from ethanol), $[\alpha]_D$ +70° (*c*, 1·33).

Methyl 16β-*Chloroeburico*-7 : 9(11)-*dien*-21-*oate* (XXXVII).—A suspension of methyl 16α-hydroxyeburico-7 : 9(11)-dien-21-oate (400 mg.) in light petroleum (40 c.c.) was shaken with phosphorus pentachloride (300 mg.) at 20° for 8 min., the ester dissolving completely. After addition of water, isolation with light petroleum yielded *methyl* 16β-*chloroeburico*-7 : 9(11)-*dien*-21-*oate* (330 mg.) as needles, m. p. 156—157° (after several crystallisations from ethanol), $[\alpha]_D$ +45° (*c*, 0·98) (Found: C, 71·3; H, 9·8; Cl, 7·25. $C_{32}H_{57}O_2Cl$ requires C, 76·35; H, 10·2; Cl, 7·05%). Light absorption: Max., 2360, 2440, and 2520 Å, ε = 13,200, 15,700, and 10,400.

Reduction of Methyl 16β-*Chloroeburico*-7 : 9(11)-*dien*-21-*oate with Lithium Aluminium Hydride.*—The ester (350 mg.) in ether (125 c.c.) was treated with lithium aluminium hydride (400 mg.) at 20° for 48 hr. Isolation as usual yielded a product (308 mg.) which was adsorbed from benzene (75 c.c.) on alumina (30 g.). Elution with benzene–ether (9 : 1; 400 c.c.) gave 16β-*chloroeburico*-7 : 9(11)-*dien*-21-*ol* (XXXVIII) (210 mg.) as needles (from methanol), m. p. 171—178°, raised by chromatographic purification and crystallisation from methanol to 177—

179°, $[\alpha]_D$ +83° (*c*, 1·08) (Found: C, 78·25; H, 10·95; Cl, 8·0. $C_{31}H_{51}OCl$ requires C, 78·3; H, 10·8; Cl, 7·5%). Light absorption: Max., 2360, 2440, and 2520 Å, ε = 13,000, 15,300, and 10,150.

Further elution with ether gave eburico-7 : 9(11)-diene-16α : 21-diol (86 mg.) as plates (from methanol), m. p. 240—244°, raised by crystallisation from ethanol to 244—247°, undepressed on admixture with an authentic sample, $[\alpha]_D$ +43° (*c*, 0·74 in pyridine). The infra-red spectrum was identical with that of an authentic sample.

Eburico-7 : 9(11) : 24(28)-*triene*-3β : 16α : 21-*triol*.—Methyl 3β : 16α-dihydroxyeburico-7 : 9(11) : 24(28)-trien-21-oate (460 mg.) in ether (100 c.c.) was heated under reflux with lithium aluminium hydride (500 mg.) for 1 hr. Isolation as usual gave *eburico*-7 : 9(11) : 24(28)-*triene*-3β : 16α : 21-*triol* as needles (375 mg.) (from methanol), m. p. 213—220°, raised by several crystallisations from methanol and ethyl acetate to 219—221°, $[\alpha]_D$ +36° (*c*, 0·99 in pyridine) (Found: C, 79·1; H, 10·4. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%). Light absorption: Max., 2370, 2440, and 2520 Å, ε = 13,200, 15,700, and 10,400.

Eburico-7 : 9(11)-*dien*-21-*ol*.—Methyl eburico-7 : 9(11)-dien-21-oate (240 mg.) in ether (30 c.c.) was treated with lithium aluminium hydride (200 mg.) at 20° for 16 hr. Isolation as usual, adsorption on alumina (20 g.), and elution with benzene–ether (9 : 1; 300 c.c.) gave *eburico*-7 : 9(11)-*dien*-21-*ol* (200 mg.) as needles (from methanol), m. p. 101—103°, raised by several crystallisations from aqueous acetone to 106—108° (after melting and resolidifying at 95—97°), $[\alpha]_D$ +62° (*c*, 1·26) (Found: C, 84·2; H, 12·0. $C_{31}H_{52}O$ requires C, 84·5; H, 11·9%). Light absorption: Max., 2360, 2430, and 2510 Å, ε = 15,000, 17,200, and 11,650.

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The Cleavage of Diaryl Ethers by Grignard Reagents in the Presence of Cobaltous Chloride. Part I. Monosubstituted Diphenyl Ethers.

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Fission of 11 monosubstituted diphenyl ethers $R{\cdot}C_6H_4{\cdot}OPh$ by a Grignard reagent in the presence of cobaltous chloride has been studied, and the resulting phenolic mixtures have been analysed. The molar ratios $R{\cdot}C_6H_4{\cdot}OH$: PhOH obtained are explained in terms of relative stability of the intermediate aryloxy-radicals. The permanent electronic effects of R can thus be evaluated.

DIPHENYL ETHER, although remarkably stable towards the usual ether-hydrolysing reagents (alkalis and Lewis acids), undergoes smooth fission by alkali metals in liquid ammonia, or somewhat less effectively, by Grignard reagents at elevated temperatures (Ungnade, *Chem. Reviews*, 1946, **38**, 405; Späth, *Monatsh.*, 1914, **35**, 319). The former reaction has been well investigated, and shown to proceed *via* intermediate anions (Sowa *et al.*, *J. Amer. Chem. Soc.*, 1937, **59**, 603, 1488; 1938, **60**, 94; cf. Birch, *J.*, 1947, 102); the latter, judged from the reaction conditions and by-products (*e.g.*, *o*-phenylphenol), appears to involve a homolytic process. Kharasch and Huang recently (*J. Org. Chem.*, 1952, **17**, 669) found that, by employing anhydrous cobaltous chloride in conjunction with a Grignard reagent, extensive cleavage of diphenyl ether can be brought about even at room temperature. The reaction in all probability involves free radicals, and atomic hydrogen has been postulated as the active agent. A study of the fission of variously substituted diphenyl ethers $R{\cdot}C_6H_4{\cdot}OPh$ by this method and analysis of the resulting phenolic mixtures ($R{\cdot}C_6H_4{\cdot}OH$ + PhOH) would reveal the effect of the substituent groups on the ether towards fission by free radicals, and thus provide information concerning the electronic

effects of such groups. In the present investigation eleven monosubstituted diphenyl ethers have been subjected to the Kharasch–Huang procedure, and the resulting phenolic mixtures analysed.

A fairly wide variety of substituents can be investigated by this method, including groups of varying combinations of moderately strong $\pm I$ and $+M$ effects. However, certain groups are outside its scope, *e.g.*, OH, NH_2, and in particular groups with a $-M$ effect such as NO_2, CO_2H, and CN, since all these are subject to attack by the Grignard reagent. The Grignard reagent–cobaltous chloride combination has been shown (Kharasch and Huang, *loc. cit.*) not to affect an alkyl aryl ether linkage (as in anisole), and so alkoxy-groups can also be studied. In view of the finding that the above combined reagents reduce bromo- and dichloro-benzene to benzene and chlorobenzene, respectively (Kharasch, Sayles, and Fields, *J. Amer. Chem. Soc.*, 1944, **66**, 481), it became necessary to ascertain whether the chlorine atom in a chlorodiphenyl ether was similarly affected. The neutral fractions from the cleavage of *o*- and *p*-chlorophenyl ether yielded no less than 72% and 74%, respectively, of the unchanged chlorodiphenyl ether while diphenyl ether was not formed to any appreciable extent; thus reduction of the chlorine atom, if it occurred at all, could not be a competing reaction.

The Grignard reagent of choice was *n*-butylmagnesium bromide, 4 mols. of which were employed with 2·5 mols. of anhydrous cobaltous chloride for each mol. of ether. The phenols produced were isolated by alkali-extraction and distilled in a partial vacuum. A forerun of approximately 5—6% was discarded, distillation being then continued until practically no residue remained. The main fraction so obtained was analysed. The estimated phenol content was thus slightly low, the maximum error being 5—6% depending on the relative volatility of the substituted phenol present. Derivatives were prepared from both fractions to establish the identity of the components.

The composition of mixtures of phenol and the methoxy- and chloro-phenols was determined by micro-Zeisel and Carius analyses. Mixtures of phenol and the cresols were analysed iodometrically, the method being based on that of Redman, Weith, and Brock (*J. Ind. Eng. Chem.*, 1913, **5**, 831), which is comparatively sensitive to presence of traces of impurities, particularly with *m*-cresol. The boiling points of these mixtures, and the fact that they readily formed pure derivatives of the respective cresols, indicated that these mixtures contained mostly the cresols, in agreement with the titrations. With a slight modification the iodometric method was found applicable to the estimation of the *o*- and *p*-chlorophenol, and the results agreed well with those obtained by microanalyses. *p-tert.*-Butylphenol and *p*-phenylphenol were isolated and weighed as such.

Experimental

Synthesis of Ethers.—Except for *o*-chlorodiphenyl ether, Ullmann and Sponagel's method (*Ber.*, 1905, **38**, 2212), using a phenol and the appropriate aryl bromide, was employed throughout: *o*-, *m*-, and *p*-methyl- and -methoxy-diphenyl ethers (Sowa *et al.*, *locc. cit.*; Lea and Robinson, *J.*, 1926, 411); *m*-chlorodiphenyl ether (from phenol, 22% yield) (Found: Cl, 16·9. Calc. for $C_{12}H_9OCl$: Cl, 17·3%) (cf. Suter and Green, *J. Amer. Chem. Soc.*, 1937, **59**, 2578); *p*-chlorodiphenyl ether (from *p*-chlorophenol, 26%) (Found: Cl, 17·1%) (cf. Brewster and Stevenson, *ibid.*, 1940, **62**, 3144); *p-tert.*-butyldiphenyl ether (from *p-tert.*-butylphenol, 55%) (Found: C, 84·8; H, 8·1. Calc. for $C_{16}H_{18}O$: C, 85·0; H, 8·0%) (cf. Pajeau, *Compt. rend.*, 1944, **218**, 236); and *p*-phenyldiphenyl ether (from phenol, 50%) (cf. Lüttringhaus and Sääf, *Annalen*, 1945, **557**, 25). *o*-Chlorodiphenyl ether was prepared from *o*-aminodiphenyl ether by a Sandmeyer reaction (Brewster and Stevenson, *loc. cit.*).

p-Chlorodiphenyl ether gave, on nitration with sulphuric–nitric acid at *ca.* 10°, a mononitro-derivative, yellow needles (from ethanol), m. p. 150—151° (Found: Cl, 14·2. Calc. for $C_{12}H_8O_3NCl$: Cl, 14·2%).

Cleavage Experiments.—The cleavage of *p*-chlorodiphenyl ether, a typical experiment, is described: *p*-Chlorodiphenyl ether (12 g., 0·06 mole) was added to the Grignard reagent prepared from *n*-butyl bromide (33 g., 0·24 mole) and magnesium (5·8 g., 0·24 mole) in diethyl ether (200 c.c.), and vigorous stirring started. Anhydrous cobaltous chloride (18 g., 0·15 mole) was then added in approx. 30 portions during 2·5 hr., at room temperature (28°). Large volumes of gases were evolved, and the mixture became black. At the end of the addition of cobaltous

chloride the mixture was stirred for a further hour, after which it was decomposed and the precipitate brought into solution by the cautious addition of water (*ca.* 75 c.c.) with external cooling, followed by 5N-sulphuric acid (*ca.* 100 c.c.). The organic layer was separated, and the aqueous layer thoroughly extracted with ether (5 × 100 c.c.). The combined extracts were washed once with dilute sulphuric acid (50 c.c.) and evaporated to *ca.* 150 c.c., and the phenols present taken up in 5% aqueous sodium hydroxide (3 × 50 c.c.). The alkali extract was washed twice with ether, acidified with 5N-sulphuric acid, saturated with sodium sulphate, and again extracted with ether (5 × 70 c.c.). After being washed with a little 20% aqueous sodium carbonate (30 c.c.) the ethereal solution was dried ($MgSO_4$) and concentrated to a crude mixture of phenols (2·4 g.) which was then distilled, giving the fractions (i) b. p. 108—114°/38 mm. (0·12 g.) and (ii) b. p. 114—136°/38 mm. (2·1 g.); there was practically no residue. Fraction (i) gave tribromophenol (m. p. and mixed m. p.); fraction (ii) gave *p*-chlorophenyl benzoate and *p*-chlorophenoxyacetic acid. The chlorine content of fraction (ii) (Found: Cl, 22·3, 22·5%) corresponded to 76 moles % of chlorophenol.

The neutral fraction was also concentrated and fractionated, giving fractions: (i) b. p. 50—84°/760 mm. (*ca.* 0·4 g.), apparently a mixture of diethyl ether and benzene; (ii) b. p. 84—102°/760 mm. (0·5 g.), consisting mainly of benzene (1 : 3-dinitro-derivative, m. p. and mixed m. p. 88—90°); (iii) b. p. 93—97°/0·7 mm. (*ca.* 0·2 g.); (iv) b. p. 97—100°/0·7 mm. (1·3 g.), n_D^{25} 1·5798; (v) b. p. 100—101°/0·7 mm. (4·5 g.), n_D^{25} 1·5839; and (vi) a dark viscous residue (1·2 g.). Fraction (v), the main fraction, was *p*-chlorodiphenyl ether (Found: Cl, 17·25%). (Note: diphenyl ether has b. p. 78°/0·7 mm., n_D^{24} 1·5826), as was the greater part of (iv), since the latter on nitration gave the mononitro-derivative of *p*-chlorodiphenyl ether (m. p. 150—151°, alone or mixed with an authentic sample prepared previously.) This brings the recovered *p*-chlorodiphenyl ether to approx. 5·8 g. (74%).

In the case of *o*-chlorodiphenyl ether, 72% of the unchanged ether was recovered as crystalline material.

In a second cleavage experiment with *p*-chlorodiphenyl ether, the phenolic mixture contained 21·7% of chlorine (73 moles % of *p*-chlorophenol; iodometric titration gave 73 moles %).

p-*Phenyldiphenyl Ether*.—The phenols produced by the cleavage of this ether (15·0 g.) were taken up in 5% aqueous potassium hydroxide (200 c.c.) which was then heated to 85° and acidified with 2N-hydrochloric acid. (Note: at 80° a 5% aqueous solution of sodium chloride dissolves 10% by weight of phenol.) The *p*-phenylphenol thus precipitated was filtered, washed with hot water, and dried (3·53 g.). The aqueous filtrate and washings, on cooling, deposited a further 0·052 g. of *p*-phenylphenol (total yield 3·58 g.; m. p. and mixed m. p. 167°). An aliquot part of the filtrate on titration with bromine indicated the presence of *ca.* 0·5 g. of phenol in all of the filtrate; actual extraction yielded 0·47 g. of phenol. Fission amounted therefore to 81 moles %.

p-tert.-*Butyldiphenyl Ether*.—Cleavage of this ether (18 g.) afforded phenolic materials which were taken up in aqueous potassium hydroxide and isolated in the usual manner, giving a liquid which readily crystallised (2·4 g.), m. p. 98—100°, alone or mixed with *p-tert.*-butylphenol.

Iodometric Titration (cf. Redman *et al.*, *loc. cit.*).—To 10 ml. of an approx. 0·03N-aqueous solution of the phenolic mixture were added 15 ml. of N-sodium hydrogen carbonate, followed by approx. 20% excess of 0·05N-iodine. The mixture was vigorously shaken for one minute, then acidified with 15 ml. of 2N-sulphuric acid, and the excess of iodine back-titrated with 0·1N-sodium thiosulphate. For mixtures of *o*- and *p*-chlorophenol and phenol, a 50—100% excess of iodine was necessary.

Results and Discussion

The results of fission experiments (Table, column 5) present a contrast to those obtained by sodium in liquid ammonia (column 6; Sowa *et al.*, *loc. cit.*). This is not unexpected considering the differing nature of the reaction mechanisms. The latter involve attack of a nucleophilic reagent, and electron-attracting groups are expected to facilitate fission on the side of the substituted ring. Thus the order of activating influence is $p\text{-}NH_2 < p\text{-}OMe < p\text{-}Me < H < p\text{-}CO_2Na$, in accordance with the known electronic effects of these groups. A free radical, however, being electrically neutral, attacks an unperturbed molecule (Waters, *Trans. Faraday Soc.*, 1941, **37**, 772; *J.*, 1948, 727); the state of polarisation of the molecule is therefore no longer important in determining the course of the reaction, and resonance-stabilisation of the reaction intermediates becomes the controlling factor. This has recently been amply demonstrated in many homolytic reactions, *e.g.*,

free-radical substitution reactions of aromatic substances, in which the nitro-group is mainly *ortho-para*-directing (Hey, Nechvatal, and Robinson, *J.*, 1951, 2892; DeTar and Scheifele, *J. Amer. Chem. Soc.*, 1951, **73**, 1442), mercuration of nitrobenzene under non-polar conditions, in which all three (*o*-, *m*-, and *p*-)positions are attacked (Klapproth and Westheimer, *ibid.*, 1950, **72**, 4461), and addition of aldehydes and polyhalogenomethanes to

Fission of $R{\cdot}C_6H_4{\cdot}O{\cdot}C_6H_5$.

R	Total fission (mole %)	Yield of $R{\cdot}C_6H_4OH$ (mole %) Iodometric titration	Microanalysis	Mean	Fission by Na–NH_3 (mole %)
o-Me	25	80	—	80	53
m-Me	36	~100	—	~100	62
p-Me	65	91	—	91	75
o-OMe	57	—	88	88	45
m-OMe	58	—	95	95	47
p-OMe	50	—	84	84 *	81
o-Cl	52	9	6	8	—
m-Cl	46	—	33	33	—
p-Cl	36, 34	—, 73	76, 73	76, 73	—
p-Bu^t	18	—	—	~100	—
p-Ph	43	—	—	81	—
p-NH_3	—	—	—	—	99
p-CO_2Na	—	—	—	—	0

* The cleavage product of this ether was described by Kharasch and Huang (*loc. cit.*) as "mostly phenol." This was based on the report (Hlasiwetz and Habermann, *Annalen*, 1875, **177**, 340), since discovered by one of us to be erroneous, that *p*-methoxyphenol was not volatile in steam. The phenolic mixture obtained was steam-distilled and the volatile fraction so obtained was titrated as phenol.

olefins in which high specificity in the direction of addition is exhibited (Patrick, *J. Org. Chem.*, 1952, **17**, 1009, 1269; Haszeldine and Steele, *J.*, 1953, 1199).

If, as postulated by Kharasch and Huang (*loc. cit.*), fission is brought about by the agency of free hydrogen atoms, two possible routes for the fission of diphenyl ether might be represented as follows:

$$C_6H_5{\cdot}O{\cdot}C_6H_5 + H{\cdot} \begin{cases} \longrightarrow C_6H_5{\cdot}O{\cdot} + C_6H_6 & \text{(i)} \\ \longrightarrow C_6H_5{\cdot}OH + C_6H_5{\cdot} & \text{(ii)} \end{cases}$$

These are not intended to depict the actual mechanism of the fission, but rather to indicate the intermediates that might be involved (see footnote, p. 674 of the preceding reference), and the isolation of benzene in addition to phenolic products in one cleavage experiment herein reported can be considered experimental evidence of the postulation of such intermediates. Of the two possible intermediates, the aryloxy- or the aryl radical, there is, apart from resonance considerations, ample experimental evidence to show that the former is comparatively much more stable. Thus, free aryls are extremely reactive (Hey and Waters, *Chem. Reviews*, 1937, **21**, 169), while aryloxy-radicals exhibit properties, *e.g.*, dimerisation (Cosgrove and Waters, *J.*, 1951, 388, 1726), consistent with a less reactive nature; in fact, certain long-lived radicals of this type have actually been prepared (*e.g.*, see Fieser and Young, *J. Amer. Chem. Soc.*, 1932, **54**, 4095). Moreover, it is well known that phenols are effective inhibitors for radical-chain reactions and the mechanism of inhibition has been shown (Waters and Wickham-Jones, *J.*, 1951, 812; 1952, 2421) to involve destruction of the chain-initiating radical R'· (*e.g.*, $C_6H_5{\cdot}$, $CH_3{\cdot}$) by a process of radical transfer with the formation of aryloxy-radicals ($R'{\cdot} + R{\cdot}C_6H_4{\cdot}OH \longrightarrow R{\cdot}C_6H_4{\cdot}O{\cdot}$) which must therefore be energetically more favourable. It follows that of the two possible routes of fission portrayed above, (i) is preferred. In a monosubstituted diphenyl ether $R{\cdot}C_6H_4{\cdot}O{\cdot}C_6H_5$, therefore, fission would take place depending on the relative stabilities of the aryloxy-radicals $R{\cdot}C_6H_4{\cdot}O{\cdot}$ and $C_6H_5{\cdot}O{\cdot}$, and substituents R which stabilise the radical $R{\cdot}C_6H_4{\cdot}O{\cdot}$ would increase the yield of $R{\cdot}C_6H_4{\cdot}OH$. Such a postulate appears to be in harmony with the results since, according to the generally accepted theory (Ingold, *Trans. Faraday Soc.*, 1934, **30**, 52), aryloxy-radicals are stabilised by electron-repelling substituents. Accordingly, *o*- and *p*-methyl as well as *o*- and *p*-methoxy-groups [all of which are electron-repelling, operating either by concerted inductive and mesomeric (hyper-

conjugative) effects ($+I$, $+M$), or by two opposing effects one of which predominates ($+M > -I$)] have all been found to lead to extensive formation of the cresols or methoxyphenols. The *m*-methyl and *p-tert.*-butyl group exemplify the effect of a purely inductive, and the *p*-phenyl a largely mesomeric, mechanism. The chloro-ethers perhaps yield results of greatest significance. Thus the cleavage product of the *meta*-isomer reflects the $-I$ effect of the *m*-chlorine atom, while the *p*-chlorine is clearly to be designated ($+M > -I$). In the case of the *o*-chlorine atom, however, although its greater inductive effect, coupled with a diminished mesomeric one, as compared with the *p*-chlorine, satisfactorily explains the reversal of the direction of cleavage, the extent to which this takes place seems too great to be accommodated by these electronic effects alone and strongly suggests that a proximity factor, the exact nature of which is yet obscure, is also in operation. The *m*-methoxy-group appears to be anomalous and no explanation can at present be given.

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The Cleavage of Diaryl Ethers by Grignard Reagents in the Presence of Cobaltous Chloride. Part II. Disubstituted Diphenyl Ethers.*

By R. L. HUANG.

[Reprint Order No. 5244.]

From relative molar yields of $R'{\cdot}C_6H_4{\cdot}OH$ against $R''{\cdot}C_6H_4{\cdot}OH$, obtained during cleavage of eleven disubstituted diphenyl ethers $R'{\cdot}C_6H_4{\cdot}O{\cdot}C_6H_4{\cdot}R''$, a scale of relative stabilising influence of various substituent groups R on the intermediate aryloxy-radical $R{\cdot}C_6H_4O{\cdot}$ has been worked out. This scale deviates from the electropositivity usually known for R in heterolytic reactions and is explained by the postulation that the stability of the aryloxy-radical is not directly measured by the electropositivity of R but to a large extent depends also on whether R offers opportunity for resonance within the radical.

IN Part I * the cleavage of monosubstituted diphenyl ethers $R{\cdot}C_6H_4{\cdot}O{\cdot}C_6H_5$ by the method indicated in the title was studied, and the results were explained in terms of the stablising effect of R on the intermediate aryloxy-radical $R{\cdot}C_6H_4{\cdot}O{\cdot}$ by which the cleavage was considered to proceed. The relative stabilising effect of R was shown to be in general agreement with Ingold's theory (*Trans. Faraday Soc.*, 1934, **30**, 52) relating the electropositivity of R to the stability of such radicals. The ratio of the amount of substituted phenol $R{\cdot}C_6H_4{\cdot}OH$ to that of phenol obtained during cleavage, which afforded a comparison of R with hydrogen in each case, should also be applicable to a comparison among the substituent groups themselves. Such a direct reference to the hydrogen of phenol, however, is practicable only in the case of the chlorodiphenyl ethers, since with all the other ethers the corresponding substituted phenols are all formed to the practical exclusion of phenol (*i.e.*, in a ratio greater than 4 : 1) and a direct comparison of such values has little quantitative significance. For such a study, competitive cleavage which leads to substantial quantities of each phenol is indicated. The present paper describes such cleavage of eleven disubstituted diphenyl ethers $R'{\cdot}C_6H_4{\cdot}O{\cdot}C_6H_4{\cdot}R''$.

Experimental.—The ethers were prepared as described previously (see Table 1 for new), *ethers* except for the ether (R′ = *m*-OMe, R″ = *p*-Cl), for which a lower reaction temperature (200°) and a longer time (4 hr.) were employed. Cleavage was effected in the usual way, except for the following ethers: (i) R′ = *p*-Cl, R″ = *m*-OMe; (ii) R′ = *p*-OMe, R″ = *p*-Bu^t; (iii) R′ = *p*-Me, R″ = *p*-C_6H_5; and (iv) R′ = *m*-Me, R″ = *p*-C_6H_5, for which in order to obtain fair

* Part I, preceding paper.

yields of the cleavage products it was necessary to use a 5-molar excess of the Grignard reagent and a 3-molar excess of cobaltous chloride.

TABLE 1. *Synthesis of disubstituted diphenyl ethers,* $R'\cdot C_6H_4\cdot O\cdot C_6H_4\cdot R''$.

R′	R″	Phenol, starting material	Yield (%)	B. p./mm. (or m. p.)	n_D^{22}	Found (%) C	H	Cl	Formula	Required (%) C	H	Cl
p-Cl	*m*-Me	*p*-Chlorophenol	43	106—107°/1	1·5776	—	—	16·4	$C_{13}H_{11}OCl$	—	—	16·2
,,	*p*-Me	,,	37	(56)	—	—	—	16·3	,,	—	—	16·2
,,	*m*-OMe	*m*-Methoxyphenol	43	119/1	1·5860	66·4	5·1	15·2	$C_{13}H_{11}O_2Cl$	66·5	4·7	15·1
,,	*p*-OMe	*p*-Chlorophenol	41	(54)	—	—	—	15·0	,,	—	—	15·1
p-OMe	*o*-Me	*o*-Cresol	49	140/1	1·5713	78·6	6·7	—	$C_{14}H_{14}O_2$	78·5	6·5	—
,,	*p*-Bu^t	*p*-*tert*.-Butylphenol	50	147—151/1	1·5545	79·9	7·8	—	$C_{17}H_{20}O_2$	79·7	7·8	—
p-Me	*p*-C_6H_5	*p*-Cresol	69	(94—96)	—	87·3	6·2	—	$C_{19}H_{16}O$	87·7	6·2	—
,,	*o*-OMe	,,	42	(51—52)	—	78·6	6·5	—	$C_{14}H_{14}O_2$	78·5	6·5	—
m-Me	*p*-C_6H_5	*m*-Cresol	76	(66—67)	—	86·8	6·2	—	$C_{19}H_{16}O$	86·7	6·2	—

Cleavage mixtures containing chlorophenols or methoxyphenols were analysed for chlorine and methoxyl, respectively; mixtures containing phenol and *p*-phenylphenol were fractionally distilled; and the mixture of *m*- and *p*-cresol was estimated iodometrically.

RESULTS AND DISCUSSION

The results of cleavage experiments are given in Table 2. By combining these with those obtained in Part I (*loc. cit.*) it is possible to prepare a list of the relative stabilising influence of various substituents R on the aryloxy-free radical $R\cdot C_6H_4\cdot O\cdot$ in terms of a stabilisation index *S* relative to hydrogen as unity (Table 3). Thus in Part I, 3·0 parts

TABLE 2. *Cleavage of ethers,* $R'\cdot C_6H_4\cdot O\cdot C_6H_4R''$.

R′	R″	Cleavage (%)	OMe (%) in phenolic mixture	$R'\cdot C_6H_4\cdot OH$ (moles %)	R′	R″	Cleavage (%)	OMe (%) in phenolic mixture	$R'\cdot C_6H_4\cdot OH$ (moles %)
p-Cl	*m*-Me	39	8·1, 8·1 *	26	*p*-OMe	*o*-Me	23	13·8	51
,,	*p*-Me	50	6·5, 6·4 *	20	,,	*p*-Me	35	8·5	31
,,	*m*-OMe	20	17·0	31	,,	*p*-Bu^t	13	9·0, 8·9	40
,,	*p*-OMe	18	14·9	39	*p*-Me	*m*-Me	14	—	62
m-Me	*p*-C_6H_5	15	—	51	,,	*o*-OMe	52	18·4, 18·1	30
					,,	*p*-C_6H_5	13	—	58

* Cl, %.

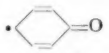
TABLE 3. *Stabilisation index (S) of substituent groups,* R.

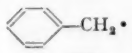
R, reference standard		Me *o*	Me *m*	Me *p*	OMe *o*	OMe *m*	OMe *p*	Cl *o*	Cl *m*	Cl *p*	Bu^t *p*	C_6H_5 *p*
H	(1·0)	—	—	—	—	—	—	0·1	0·3	3·0	—	—
p-Cl	(3·0)	—	8·6	12	—	6·7	4·7	—	—	—	—	—
p-OMe	(4·7)	4·5	—	11	—	—	—	—	—	—	7·1	—
p-Me	(12)	—	7·3	—	28	—	5·4	—	—	—	—	8·7
p-C_6H_5	(8·7)	—	8·8	—	—	—	—	—	—	—	—	—

of *p*-chlorophenol to one part of phenol were obtained from *p*-chlorodiphenyl ether; hence for the *p*-chlorine atom, $S = 3·0$ (first row). With *p*-chloro-*p*′-methoxydiphenyl ether, the yield of *p*-cresol is 61%, and hence for *p*-methoxy-, $S = 61/39 \times 3·0 = 4·7$. Similarly for *p*-methyl, $S = 80/20 \times 3·0 = 12$ (second row). With these subsidiary standards the figures for the other substituents in the third and the fourth row are calculated. The *m*-methyl group was further checked against *p*-phenyl (fifth row). It is seen that, where more than one standard was used for a particular substituent, the values obtained checked well with each other (*m*- and *p*-methyl and *p*-methoxy-).

Although considerable chemical evidence existed, and was advanced in Part I, to support the postulate that free aryloxy-radicals $R\cdot C_6H_4\cdot O\cdot$ are relatively more stable than aryl radicals $R\cdot C_6H_4\cdot$, and that consequently cleavage should proceed *via* the former rather

than the latter, it seems desirable, in view of the fact that this postulate forms the basis of the proposed cleavage mechanism, to find further support from a consideration of the relative energies of such radicals. In the equilibrium $C_6H_5{\cdot}O{\cdot} + C_6H_5{\cdot}H \rightleftharpoons C_6H_5{\cdot}OH + C_6H_5{\cdot}$, the left- or right-hand side is favoured according to whether the phenoxy- or the phenyl radical, respectively, is the more stable. A consideration of bond energies alone would lead to the conclusion that the right-hand side is favoured, since the bond energy of the O–H linkage is 110 kcal. and that of the C–H linkage is only 87 kcal. However, resonance between structures such as (I) as well as the Kekulé structures should, by analogy with the free benzyl radical, stabilise the phenoxy-radical by about 20 kcal.


(I)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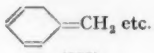
(III)

(Szwarc, *J. Chem. Phys.*, 1948, **16**, 128). Moreover, Pullman (*Discuss. Faraday Soc.*, 1947, **2**, 26) has calculated that in the free benzyl radical, (II) makes a 62·8% contribution and (III) 37·2%. If these proportions hold for the phenoxy-radical, then the replacement of the =C by the =O linkage should give a further 15 kcal. Hence in the reaction above the left-hand side is favoured to an extent of approximately 12 kcal., *i.e.*, the phenoxy-free radical is the more stable.

If it is accepted that aryloxy-radicals are the intermediates in the cleavage, and that substituents act mainly electropositively in stabilising such radicals (Ingold, *loc. cit.*), the values obtained in Table 3 might constitute a measure of the relative polarisation effects of R in the radicals. Thus from the data it would be concluded that : (*a*) the electronic effect of the *p*-chlorine atom is $(+M > -I)$, and that $+M$ is considerable in magnitude, by comparison with the value obtained for the *m*-chlorine atom (factor of **10 : 1**); (*b*) that in the *p*-phenyl group, the preponderance of the $+M$ effect over $-I$ is even more pronounced; (*c*) that the *p*-methyl group is more electron-releasing than either the *m*-methyl or the *p-tert.*-butyl group, in spite of the greater $+I$ effect which the last two groups possess (this result would have to be attributed solely to hyperconjugation of the *p*-methyl group); (*d*) that the *p*-methoxy-group has a greater tendency for electron-release than hydrogen $(+M > -I)$, as is well known, but that this tendency in the radical is smaller than that of the *p*-methyl group; (*e*) that the value for the *o*-methoxy-substituent appears abnormally high, and that of the *o*-chloro- extremely low; (*f*) that the *m*-methoxy-group does not exhibit the effect usually attributed to this group, namely, $-I$.

These observations in many respects deviate from the results obtained by the well-known acid–base equilibria measurements, *e.g.*, in the thermodynamic dissociation constants of substituted acetic and benzoic acids (see Ingold, " Structure and Mechanism in Organic Chemistry," Bell & Sons, 1953, pp. 722—750), from which it is known that (*a*) the electronic effect for the *p*-chlorine atom is $(-I > +M)$, (*b*) that for *m*-methoxy is $-I$, and (*c*) that in electropositivity the *p*-methoxy-group is greater than the *p*-methyl group. The stabilising influence of R, if taken as a direct measure of the electropositivity, would also appear too large for (*a*) the *p*-methyl group, as compared with *m*-methyl and *p-tert.*-butyl, since the hyperconjugative effect is usually known to be relatively small, and (*b*) the *p*-phenyl substituent which recent measurements on the dissociation constant of diphenyl-4-carboxylic acid (Berliner and Blommers, *J. Amer. Chem. Soc.*, 1951, **73**, 2479) show to be only weakly $(+M > -I)$.

Most of these apparent irregularities can be explained if it is postulated that the stability of the free aryloxy-radical is not dependent on the electropositivity of R as measured in heterolytic reactions, but to a large extent depends also on whether R offers opportunity for resonance within the radical itself. Thus in cases where only the inductive effect $+I$ operates, the radical is stabilised, hence the observed values for the *m*-methyl and *p-tert.*-butyl groups; where both the inductive and the mesomeric mechanisms are operative, however, the latter would appear to play a more decisive rôle, hence the relatively large values for the *p*-methyl and *p*-phenyl groups, as well as the stabilising effect of the *p*-chlorine atom. When viewed in this light, the *o*-methyl group, which possesses a greater

$+I$ and a smaller $+M$ effect than *p*-methyl, also gives a value for S of the correct order, and suggests that the proximity factor responsible for the abnormal figures for the *o*-methoxy- and *o*-chloro-substituents is not entirely a steric one. No explanation can be offered for the greater S value of the *p*-methyl than of the *p*-methoxy-, and for the abnormally large one of the *m*-methoxy-group.

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*The Influence of the Nitro-group on the Reactivity of Aromatic Halogens. Part II.**

By C. W. L. BEVAN and G. C. BYE.

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Relative rates and Arrhenius parameters have been determined for the reactions with methoxide ion in " AnalaR " methanol of a series of mono- and di-nitrofluorobenzenes. The results permit a quantitative comparison of activation, in aromatic nucleophilic substitution, from the *meta*-position with that from other positions. The relative constancy of the non-exponential term of the Arrhenius equation over a very wide range of reaction rates is noted.

THE relative rates of electrophilic substitution at the three possible positions in mono-substituted benzenes have been extensively studied by Hughes, Ingold, and their collaborators (cf. Ferguson, *Chem. Reviews*, 1952, **50**, 47), but the corresponding nucleophilic substitution is by no means so extensively documented (cf. Bunnett and Zahler, *ibid.*, 1951, **49**, 273). Arrhenius parameters were therefore determined for an exchange reaction involving replacement of the fluorine atom of *o*-, *m*-, and *p*-fluoronitrobenzenes since data hitherto available do not permit quantitative comparison between activation, in such substitutions, from the *meta*-position with that from other positions.

The methoxide ion was chosen as the replacing entity since it is less likely than the ethoxide ion to cause steric complications and its reactions with halogenonitrobenzenes are less complex; the ethoxide ion can cause reduction of such compounds (Lobry de Bruyn, *Rec. Trav. chim.*, 1890, **9**, 197), whereas methoxide ion gives with *m*-fluoronitrobenzene a quantitative yield of *m*-nitroanisole (Holleman and Beekman, *ibid.*, 1904, **23**, 225).

It was also of interest to see whether *m*-fluoronitrobenzene gave a straightforward bimolecular reaction with methoxide ion since Kristjansen and Winkler (*Canad. J. Chem.*, 1951, **29**, 154) found the exchange reaction of sodium iodide with *m*-iodonitrobenzene in acetonitrile gave better first- than second-order rate constants.

Finally one of the basic assumptions on which theoretical calculations of such relative reactivities are based (cf. Dewar, *J.*, 1949, 463; Sixma, *Rec. Trav. chim.*, 1953, **72**, 4, 273) is that differences in reaction rates are due only to activation energy differences: this has not hitherto been tested for nucleophilic displacements at an aromatic carbon atom, in a series which includes unactivated and *meta*-activated cases. Thus Arrhenius parameters were also determined in the analogous reactions of 1-fluoro-2 : 4-dinitrobenzene, fluorobenzene, and 1-fluoro-3 : 5-dinitrobenzene.

Results.—Rate constants are assembled in Table 1. Comparative rate constants at 49·5° and Arrhenius parameters are shown in Table 2.

The results obtained in a typical run with *m*-fluoronitrobenzene are given in Table 3 and the influence of the initial concentration of reagents on k_2 in this run is shown in Table 4. The value of k_2 evidently depends in a simple manner on the concentration of the fluoride

* Part I, *J.*, 1951, 2340.

and of the methoxide ion. The slight variation in rate constants is attributable to a salt effect.

The reaction of 1-fluoro-3 : 4-dinitrobenzene with methoxide ion in absolute methanol leads to the formation of 2 : 4-dimethoxynitrobenzene but an analysis of the four possible reactions involved has not yet been carried out.

By analogy with *m*-nitroanisole, the nitration of *m*-fluoronitrobenzene might have been expected to occur mainly in the 2-position (cf. Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 268). However the direction of substitution is controlled by the $-I$ effect of fluorine as would be expected from the *ortho-para* ratio in the nitration of fluorobenzene (cf. Ingold, *op. cit.*, p. 261).

TABLE 1. k_2 (*l. sec.*$^{-1}$ *mole*$^{-1}$) *for* 1-*fluoronitrobenzenes with* OMe^- *in " AnalaR " methanol.*

Substituent	Nil		2-nitro-			
Temp.	117·5°	149·1°	49·51°	38·98°	28·17°	17·90°
k_2	$6{\cdot}20\times10^{-6}$	$2{\cdot}07\times10^{-5}$	$1{\cdot}60\times10^{-3}$	$5{\cdot}66\times10^{-4}$	$1{\cdot}78\times10^{-4}$	$5{\cdot}62\times10^{-5}$

Substituent	3-nitro-				4-nitro-			
Temp.	97·87°	112·45°	119·92°	129·40°	49·54°	38·99°	28·52°	17·95°
k_2	$5{\cdot}73\times10^{-5}$	$2{\cdot}50\times10^{-4}$	$5{\cdot}13\times10^{-4}$	$1{\cdot}23\times10^{-3}$	$2{\cdot}37\times10^{-3}$	$8{\cdot}16\times10^{-4}$	$2{\cdot}68\times10^{-4}$	$7{\cdot}92\times10^{-5}$

Substituent	2 : 4-dinitro-		3 : 5-dinitro-			
Temp.	−21·3°	−1·5°	49·56°	39·15°	29·00°	17·97°
k_2	$2{\cdot}57\times10^{-1}$	$1{\cdot}55\times10^{0}$	$4{\cdot}19\times10^{-3}$	$1{\cdot}36\times10^{-3}$	$4{\cdot}21\times10^{-4}$	$1{\cdot}07\times10^{-4}$

TABLE 2. k_2 (*l. sec.*$^{-1}$ *mole*$^{-1}$) *at* 49·55° *and Arrhenius parameters* ($k_2 = Be^{-E/RT}$).

Substituent	Nil	3-nitro	2-nitro	4-nitro	3 : 5-dinitro	2 : 4-dinitro
k_2	$3{\cdot}38\times10^{-12}$	$1{\cdot}59\times10^{-7}$	$1{\cdot}60\times10^{-3}$	$2{\cdot}37\times10^{-3}$	$4{\cdot}19\times10^{-3}$	$5{\cdot}66\times10^{1}$
log B	13·0	12·8	10·7	11·0	12·3	10·1
E (kcal.)	36·4	28·9(±0·3)	19·9(±0·2)	20·1(±0·2)	21·7(±0·2)	12·3(±0·3)

TABLE 3. *Determination of rate constants* k_2 (*l. sec.*$^{-1}$ *mole*$^{-1}$).

Reaction of *m*-fluoronitrobenzene with sodium methoxide in absolute methanol. Initially, [Halide], ≈ 0·03M and [NaOMe] ≈ 0·04M. Concn. are expressed in ml. of 0·0260N-NaOEt per 9·80 ml. of sample. Temp., 112·45°.

t (min.)	0	255	490	670	1395	1575	1942
NaOMe	13·32	12·07	11·17	10·58	8·72	8·37	7·77
Halide	11·36	10·11	9·21	8·62	6·76	6·41	5·81
10^4k_2	—	2·26	2·20	2·18	2·20	2·19	2·17

t (min.)	2118	2835	3095	3308	3570	4320	4615	∞
NaOMe	7·49	6·61	6·43	6·12	5·93	5·30	5·08	1·96
Halide	5·53	4·65	4·47	4·16	3·97	3·34	3·12	0·00
10^4k_2	2·19	2·18	2·12	2·20	2·17	2·25	2·28	—

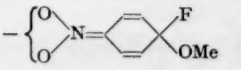
Mean $k_2 = 2{\cdot}20 \times 10^{-4}$; corrected value for solvent expansion (16—112°) $k_2 = 2{\cdot}50 \times 10^{-4}$.

TABLE 4. *The effect of variation of concentration* (*mole l.*$^{-1}$) *of reagents on* k_2 (*Temp.*, 129·4°).

NaOMe	0·068	0·040	0·033	0·017	0·017
Fluoride	0·030	0·017	0·032	0·017	0·030
10^3k_2	1·12	1·24	1·22	1·33	1·32

Discussion.—The most striking point about the results shown in Table 2 is that the rate constants vary over a range of 10^{13} with a corresponding variation of activation energy between 12 and 36 kcal., while the non-exponential factor only varies by a factor of the order of 10^3. The figures justify the assumption that in the absence of steric effects substituent groups in aromatic substitution influence reaction rates at positions *ortho*, *meta*, and *para* to themselves mainly by their effect on activation energies. The non-exponential factors decrease in the same sequence as the activation energies but there does not appear to be a simple relationship between them. However, though interpretations of differences of this order on the basis of a few observations have limited significance, the non-exponential factor in the un- and two *meta*-activated cases (~12·5) is a couple of powers of ten

greater than that of the *ortho-*, *para-*, and 2 : 4-di-substituted (~10·5). This may be attributable to a considerably greater contribution of quinonoid structures (*e.g.* as inset)



in the transition states of the latter leading to more precise geometrical requirements with respect to entering and expelled groups than in the former, the transition states of which more closely resembling the aliphatic case, involve two less precisely defined partial bonds. Further, the charge on the transition state in the latter group is less dispersed than in the former compounds because of resonance involving structures such as that illustrated. The initial states of both are, to a first approximation, equally solvated and more so than the transition states where the charge on the methoxide ion is dispersed. Thus the exp ($\Delta S/\boldsymbol{R}$) term of the transition-state equation should be greater in the *meta-* and un-substituted compounds, leading to a higher probability factor, as is in fact observed (cf. Gripenberg, Hughes, and Ingold, *Nature*, 1948, **161**, 480).

A further point emerges when one considers the additive effects of substituents. Thus the introduction of a *m*-nitro-group into fluorobenzene reduces the activation energy for the replacement considered here by 7 kcal., and the introduction of a second *m*-nitro-group, to give 1-fluoro-3 : 5-dinitrobenzene, causes a further reduction by 7 kcal., while in all three reactions the non-exponential factor is sensibly constant. However this additivity does not obtain as between the independent facilitation by *o-* and *p*-nitro-groups (~16 kcal.) and that effected by both simultaneously in 1-fluoro-2 : 4-dinitrobenzene (~24 kcal.). This is a further example of an apparent limit to the capacity of the benzene ring for transmission of the electrical influences from powerfully perturbing groups to the seat of reaction (cf. Newton, Stubbs, and Hinshelwood, *J.*, 1953, 3384).

Experimental

Materials.—Fluorobenzene. A commercial specimen after fractionation had b. p. 85·0° (uncorr.).

1-*Fluoro*-3 : 4-*dinitrobenzene.* This was prepared in about 70% yield by nitration of 1-fluoro-3-nitrobenzene in nitric–sulphuric acid. After repeated recrystallisation from ethanol the product had m. p. 49·5°. Reaction with methoxide ion in absolute methanol (two equivalents of sodium methoxide were used in 12 hr. at 80·6°) gave a product, m. p. 74·5°; 3 : 4-dinitroanisole, prepared as described by Vermuelen (*Rec. Trav. chim.*, 1906, **25**, 30), had m. p. 74·1°. The identity is confirmed by the work of Suschitzky (*J.*, 1953, 3042).

1-*Fluoro*-3-*nitrobenzene and* -4-*nitrobenzene.* These were prepared by Schiemann's method (*Ber.*, 1929, **62**, 3041) from the corresponding nitroanilines. The former was fractionated and had b. p. 198·0° (uncorr.); the latter was recrystallised from absolute ethyl alcohol to constant m. p. 26·8°.

1-*Fluoro*-2-*nitrobenzene.* This was prepared from fluorobenzene by Swarts's method (*Rec. Trav. chim.*, 1913, **33**, 263) and fractionated at 22 mm.; it had m. p. −5·3°.

1-*Fluoro*-3 : 5-*dinitrobenzene.* 3 : 5-Dinitroaniline, made from 3 : 5-dinitrobenzoyl chloride by the method of Blanksma and Verberg (*ibid.*, 1934, **53**, 988), was converted by Schiemann's method (*loc. cit.*) into 1-fluoro-3 : 5-dinitrobenzene, which was recrystallised from light petroleum (b. p. 80—100°) to a constant m. p. of 43·6°.

1-*Fluoro*-2 : 4-*dinitrobenzene.* A commercial specimen was crystallised from ether to constant m. p. 26·0°.

Methanol. Magnesium (10 g.) and iodine (0·5 g.) were dissolved in "'AnalaR" methanol (2 l.) which was then refluxed for ½ hr. and distilled.

Kinetic Measurements.—Thermostat temperatures below 100° were steady to within ±0·02°, those above 100° to within ±0·05°. The reactions were carried out in well-stoppered flasks below 50°, and above this temperature in sealed tubes. In all solutions except those of fluorobenzene and 1-fluoro-2 : 4-dinitrobenzene, sodium methoxide was ~0·03M and the halide ~0·02M. With fluorobenzene both concentrations were raised by a factor of 5 and with the 1-fluoro-2 : 4-dinitro-compound both concentrations were 0·002M. The reactions were followed by the procedure used by Bevan (*J.*, 1953, 655) except in the case of fluorobenzene where the reaction was very slow and, since the possibility of side reactions cannot be excluded, the initial rate of production of fluoride ion was measured by Rowley and Churchill's method (*Ind. Eng. Chem. Anal.*, 1937, **9**, 551) and was assumed to be due to replacement by methoxide ion. Rate con-

stants in this case decreased as reaction proceeded so that in order to get an estimate of the Arrhenius parameters, rate constants were used which had been calculated after the same percentage reaction at two temperatures.

One of us (G. C. B.) thanks the Council of University College, Exeter, for a Scholarship, during the tenure of which this work was carried out.

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The Anodic Oxidation of Metals at Very Low Current Density. Part IV. Palladium.*

By S. E. S. EL WAKKAD and A. M. SHAMS EL DIN.

[Reprint Order No. 5122.]

Little work had been done on the anodic oxidation of palladium, and the results are conflicting. These have been clarified by studying the anodic oxidation of palladium in solutions of varying pH values at very low current density. It is shown that $Pd(OH)_2$ is first formed on the surface of palladium in the form of a layer less than unimolecular, followed by $Pd(OH)_4$ at the oxygen-evolution potential. The latter hydroxide or oxide is unstable, decomposing to $Pd(OH)_2$.

THE results of previous work on the anodic oxidation of palladium are conflicting. Jirsa (*Z. Physik*, 1921, **213**, 241) suggested the formation of the oxides Pd_2O, PdO, PdO_2, and PdO_3 on the palladium anode. Müller and Riefkohl (*Z. Elektrochem.*, 1928, **34**, 744; 1930, **36**, 181) believed PdO to be the only oxide formed on the palladium anode. Butler and Drever (*Trans. Faraday Soc.*, 1936, **32**, 427), on the other hand, showed that at quite low current density an adsorbed single layer of oxygen was formed on the anode before evolution of oxygen; at high current density a less than unimolecular layer of the oxide was formed. This oxide was considered to be a peroxide which decomposed spontaneously after the interruption of the current.

In the present investigation this point is clarified by studying the anodic oxidation of palladium at very low current density, El Wakkad and Emara's procedure (*J.*, 1952, 461; 1953, 3504, 3508) being used. With an electrode of large surface area and a very small polarising current, a considerable time is required for the electrode to pass from the hydrogen- to the oxygen-evolution values, and so equilibrium potentials can be measured at each stage of the polarisation. From such a study it is shown that $Pd(OH)_2$ is first formed over the surface of palladium in a layer less than a unimolecular. This is followed by $Pd(OH)_4$ which is formed at the oxygen-evolution potential. The latter hydroxide or oxide is unstable, decomposing to $Pd(OH)_2$.

EXPERIMENTAL

The electrical circuit and the electrolytic cell used were the same as previously used by El Wakkad and Emara (*locc. cit.*). The palladium electrodes were prepared by palladising a platinum foil of 2 sq. cm. apparent area with a smooth and then with a spongy layer. This was carried out in 1% palladium chloride solution in 0·25N-hydrochloric acid. The smooth palladium layer was deposited with a current of 2·5 mA per electrode for 40 min. This was followed by deposition at 150 mA for a further 2 min. to form a spongy layer.

The electrode was washed several times with conductivity water, and then with the solution in which it would be studied, before it was introduced in its compartment in the electrolytic cell. The anode was placed in such a position with respect to the cathode as to ensure uniform distribution of the polarising current at the anode surface. Each experiment was carried out with a freshly prepared electrode.

* Part III, *J.*, 1953, 3508.

Measurements have been carried out mainly with three electrolytes representing the acid, the neutral, and the alkaline pH range. These solutions were 0·1N-sulphuric acid, 0·2M-KH_2PO_4 + 0·2M-Na_2HPO_4 buffer mixture of approximate pH 6·8, and 0·1N-sodium hydroxide, all prepared from " AnalaR " materials and conductivity water. The solution in the cell was boiled before use and cooled in an atmosphere of pure nitrogen to remove any dissolved oxygen.

The current used was 50 μA per electrode. In each solution three studies were carried out on each electrode—anodic polarisation, cathodic polarisation, and anodic decay.

In the case of the anodic polarisation, the electrode was first polarised cathodically at a current of 2 mA/electrode until hydrogen was evolved and a constant potential was recorded. The polarising current was then reversed to start the anodic polarisation, and owing to the high adsorptive power of palladium for hydrogen, the anodic polarisation started with a polarising current of 1 mA per electrode. The anode potential under these conditions was found to be constant, indicating the removal of the adsorbed hydrogen formed during the cathodic polarisation. This process was continued until the potential of the anode started to change towards more positive values, indicating the approach of the end of this process. The polarising current was then reduced to the value at which the anodic polarisation was required, and the potential of the anode was recorded as a function of time. The cathodic curves were obtained after the electrode had been anodically polarised until oxygen was evolved; the current was then reversed and the potential of the working electrode was measured at suitable times. In the case of anodic decay curves, the electrode was polarised anodically until oxygen was evolved. The current was then interrupted and the potential was measured after various times. All experiments were carried out in an atmosphere of pure nitrogen.

The reference half-cell was a saturated calomel electrode prepared according to Harned and Owen (" The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, 1943, p. 321). The electrolytic cell and the reference half-cell were kept in an air-thermostat at 25° ± 0·01°. The E.M.F. was measured with a Tinsley potentiometer provided with a Tinsley mirror-galvanometer.

Results and Discussion

Curves *A*, in Figs. 1, 2, and 3, are respectively the characteristic anodic polarisation curve of the palladium electrode at 25° with a polarising current of 50 μA in 0·1N-sulphuric acid, the same anodic polarisation curve in phosphate buffer of pH 6·8, and the anodic polarisation curve in 0·1N-sodium hydroxide. From these curves, which show the variation of the potential of the palladium anode with the quantity of electricity passed, it can be seen that the following three stages take place as the palladium electrode is forced from the hydrogen-evolution to the oxygen-evolution potential.

(*a*) A comparatively long period of constant potential (represented by the dotted line since in this case the polarising current was 1 mA to enhance the removal of the adsorbed hydrogen as was explained before), followed by a slow and somewhat irregular but reproducible rise of potential. (*b*) A rapid build-up of potential. (*c*) A somewhat slow rise of potential accompanied by two steps, the second of which coincides with the potential of oxygen evolution. Stage (*a*) can be attributed to the ionisation of adsorbed hydrogen formed during the cathodic polarisation of the electrode before the anodic polarisation was started. The quantity of electricity passed in this step was very reproducible, amounting to ~1800 mc per electrode in acid medium, and ~1300 mc per electrode in neutral and alkaline solutions; these are respectively equivalent to $1·13 \times 10^{19}$ and $8·2 \times 10^{18}$ atoms of hydrogen. These quantities were found to be independent of the quantity of electricity passed during the previous cathodic polarisation so long as this was greater than 1800 mc per electrode in acid medium, and 1300 mc in neutral and alkaline solutions.

On preparing several palladium electrodes under the standard conditions and determining the quantity of palladium present on each electrode by means of dimethylglyoxime, an average value of 0·0019 g. of palladium per electrode was obtained. This is equivalent to $1·09 \times 10^{19}$ atoms of palladium present on each electrode. From these results, it is clear that in acid medium during the cathodic polarisation, the electrode has been transformed to the hydride PdH. The presence of such a hydride was reported by Paal and Gerum (*Ber.*, 1908, **41**, 818).

In neutral and alkaline solutions, on the other hand, the atomic ratio Pd : H is about

1 : 0·7; this, together with the reproducibility of the results, suggests the approach of the formation of the hydride Pd_2H rather than PdH. The presence of the hydride Pd_2H was reported by Gillespie and Hall (*J. Amer. Chem. Soc.*, 1926, **48**, 1207), and by Hanawalt (*Proc. Nat. Acad. Sci.*, 1928, **14**, 953) in his study on the effect of hydrogen on the *X*-ray absorption spectrum of palladium.

Stage (*b*) can be ascribed by analogy, from the previous studies (El Wakkad and Emara, *locc. cit.*), to the charging of a double layer. Measurement of a large number of polarisation curves in 0·1N sulphuric acid gave an average value of the double layer capacity of

FIG. 1.

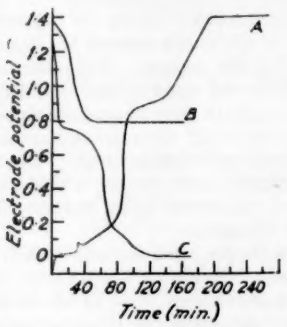


FIG. 2.

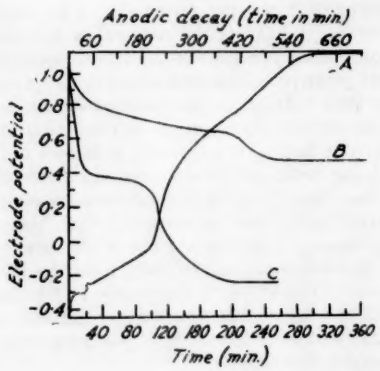
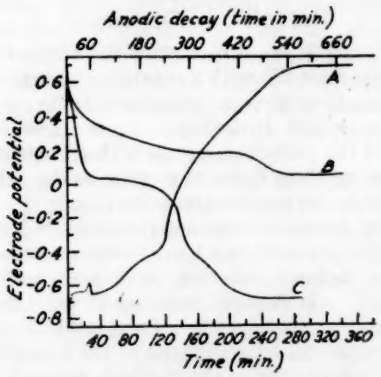


FIG. 3.



14,175 μF per apparent sq. cm. of our palladium electrode. In phosphate buffer and sodium hydroxide solution the average value was 72,000 μF per apparent sq. cm. The difference can be attributed to the fact that in acid solution the metallic surface was obtained from the oxidation of the hydride PdH, while in the neutral and alkaline solutions the hydride was Pd_2H, as has been shown above. According to Thoma (*Z. physikal. Chem.*, 1889, **3**, 69), palladium electrolytically charged with hydrogen expands equally in all directions; on subsequent removal of hydrogen, the contraction is greater than the previous expansion.

The characteristics of stage (*c*) in the anodic polarisation curves are of great interest. The onset of this stage is well defined in acid medium, but less clear in neutral or alkaline solutions. Thus, after the charging of the double layer, the first step in this stage started at potentials of +0·85, +0·47, and +0·12 v for 0·1N-sulphuric acid, phosphate buffer, and 0·1N-sodium hydroxide solutions, respectively. In the following table the starting potentials of this step in the various electrolytes are compared with the corresponding

equilibrium potentials of the system Pd–$Pd(OH)_2$. The latter values were obtained as follows: The free energy of palladous hydroxide being taken as −70,500 cal., and that of OH^- ions as −37,583 cal. (Latimer, "The Oxidation States of the Elements and their Potentials in Aqueous Solutions," New York, 1938, p. 190), the free energy change of the reaction $Pd + 2OH^- = Pd(OH)_2 + 2e$ is $\Delta F = +4670$ cal., and hence $E_B°$ (the potential value at the extreme alkaline range of pH) is *ca.* +0·10 v at 25°. By applying the ordinary equation for the variation of the potential of this system with the pH, the values obtained in col. 3 in the following table are obtained. The very close agreement between these two sets of values strongly suggests that the onset of stage (*c*) corresponds to the commencement of formation of palladous oxide or hydroxide on the palladium surface.

Solution	Starting potential of the 1st arrest, v	Equilibrium potential of system Pd–$Pd(OH)_2$, v
0·1N-H_2SO_4	+0·85	+0·88
Phosphate buffer	+0·47	+0·52
0·1N-NaOH	+0·12	+0·16

The quantity of electricity passed from the beginning to the end of the first step was ~120,000 μC in acid solution, and about ~280,000 μC in neutral and alkaline solutions. The quantity of electricity passed in acid medium and in neutral or alkaline solution is sufficient for the liberation of $3·7 \times 10^{17}$ and 9×10^{17} atoms of oxygen, respectively. If the diameter of the palladium atom is taken as $2·44 \times 10^{-8}$ cm. (from the specific gravity) there should be about $1·68 \times 10^{15}$ atoms of metal per true sq. cm. at the palladium surface. A rather rough estimate for the ratio of the real to the apparent area of the palladium electrode under investigation can be obtained from the value of the capacity of the double layer at the electrode. The capacity of a metal anode before oxide formation was estimated as 100 μF per true sq. cm. (El Wakkad and Emara, *loc. cit.*). This gives the real area of our palladium electrode (of 2 sq. cm. apparent area) as 284 sq. cm. in sulphuric acid, and 1450 sq. cm. in both phosphate and sodium hydroxide solutions. This shows that the quantity of electricity passed in the first step corresponds to the formation of less than a unimolecular layer of $Pd(OH)_2$ on the surface of palladium electrode in all the solutions.

From thermal data, Latimer (*op. cit.*) calculated the $E_B°$ value for the reaction $2OH^- + Pd(OH)_2 = Pd(OH)_4 + 2e$ as +0·71 v.

It is interesting to find that by applying the ordinary equation for the variation of the potential of such a system with pH, and comparing these values with our constant potential values found in the anodic polarisation curves at oxygen evolution, the results shown in the following table were obtained. It is clear that the equilibrium potentials for the system

Solution	Potential (v) obtained from polarisation curves	Equilibrium potential (v) for system $Pd(OH)_2$–$Pd(OH)_4$
0·1N-H_2SO_4	1·44	1·49
Phosphate buffer	1·12	1·13
0·1N-NaOH	0·72	0·77

$Pd(OH)_2$–$Pd(OH)_4$ are in good agreement with those obtained from polarisation curves, which suggests that oxygen evolution can be attributed to the formation of the higher oxide or hydroxide $Pd(OH)_4$, and, as this potential value is always constant and independent of the time of polarisation as well as of the current density (since a 100-fold increase of the polarising current was accompanied only by an increase of 200 mv in the oxygen evolution potential), it can be concluded that $Pd(OH)_4$ is unstable, giving off oxygen as soon as it is formed by the anodic polarisation. This conclusion can be further proved from both the decay and the cathodic curves. Thus, from curves *B*, Figs. 1, 2, and 3, it can be seen that on interruption of the polarising current when the anode is at the oxygen-evolution potential, the potential did not drop directly to that of the system Pd–$Pd(OH)_2$, but halted for some time at the oxygen-evolution potential or the potential of $Pd(OH)_2$–$Pd(OH)_4$, confirming the existence of the higher oxide or hydroxide over the electrode. However, after a time which varied from one solution to another, as well as the duration of electrolysis after the electrode had attained the value of the oxygen evolution, the potential dropped further to the Pd–$Pd(OH)_2$ value, showing that the $Pd(OH)_4$ formed on the surface of the electrode during its anodic polarisation was rather unstable.

In the cathodic curves *C*, Figs. 1, 2, and 3, there are also clear steps indicating the reduction of $Pd(OH)_4$ and $Pd(OH)_2$ at their corresponding reversible potential values, and confirming the formation of these two oxides or hydroxides on the palladium electrode as revealed by the anodic curves.

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The Anodic Oxidation of Metals at Very Low Current Density. Part V. Gold.*

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[Reprint Order No. 5123.]

The results of various workers on the variation of the anode potential with the quantity of electricity passed when the gold electrode is forced from hydrogen to oxygen evolution, as well as on the type of oxide formed on the surface of the metal before oxygen evolution, are not in agreement. These are clarified in this investigation by studying the anodic oxidation of gold in acid, neutral, and alkaline solutions at very low current density. It is shown that Au_2O is first formed on the anode, then AuO, and lastly Au_2O_3 before oxygen evolution. No evidence has been obtained for the presence of the oxide AuO_2.

THE results of various workers on the anodic oxidation of gold as well as the type of oxides formed on the surface of the metal before oxygen evolution are not in agreement. Jeffery (*Trans. Faraday Soc.*, 1915, **11**, 9), studying the electrolysis of nitric, sulphuric, and orthophosphoric acids with gold anodes, reported separation of a brown mixture of hydrated Au_2O and Au_2O_3. Jirsa and his co-workers (Jirsa and Buryanek, *Chem. Listy*, 1922, **16**, 189, 299, 328; *Z. Elektrochem.*, 1923, **29**, 126; Jirsa and Jelinek, *Chem. Listy*, 1924, **18**, 1; *Z. Elektrochem.*, 1924, **30**, 286, 534) showed that Au_2O, Au_2O_3, and AuO_2 were formed on gold anodes in solutions of sulphuric acid. The dissociation pressure of the oxide AuO_2 was considered to be above 1 atm., so that it liberated oxygen and formed Au_2O_3. Shutt and his co-workers (Shutt and Stirrup, *Trans. Faraday Soc.*, 1930, **26**, 635; Shutt and Walton, *ibid.*, 1932, **28**, 740; 1933, **29**, 1209; 1934, **30**, 915) found that when gold was anodically polarised in sulphuric acid Au_2O_3 was formed, but in hydrochloric acid Au_2O_4 was the only oxide formed. The thickness of the oxide film in both cases was 1—2 molecules. Armstrong, Himsworth, and Butler (*Proc. Roy. Soc.*, 1933, **143**, *A*, 89), using moderate current densities and a string galvanometer as an indicating instrument, found that in 0·1M-sulphuric acid there were two stages in the polarisation—the first rapid, linear change was attributed to the charging of a double layer, and the second, gradual rise of potential starting from +1·27 v was considered to represent the formation of auric oxide initially as a unimolecular layer. In 0·1M-sodium hydroxide the stages were less distinct, but from the quantity of electricity passed, it was concluded that at a potential of ~+0·5 v the adsorption of a single layer of oxygen atoms took place.

Deborin and Erschler (*Acta Physicochem. U.S.S.R.*, 1940, **13**, 347), on the other hand, concluded that the anodic oxidation of a gold surface leads to the formation of a layer of 0·5—1 oxygen atom adsorbed on the surface. Hickling (*Trans. Faraday Soc.*, 1946, **42**, 518), using his oscillographic method, showed that Au_2O_3 was formed as a unimolecular film on the surface of the anode before oxygen evolution.

We have now studied the anodic oxidation of gold at very low current density in acid, neutral, and alkaline solutions, and show that Au_2O is first formed on the anode, followed by AuO and then Au_2O_3 before evolution of oxygen. No evidence has been obtained for the presence of the oxide AuO_2.

* Part IV, preceding paper.

Experimental

The electrical circuit and the electrolytic cell employed were as described by El Wakkad and Emara (*J.*, 1952, 461; 1953, 3504, 3508). The gold anode was prepared by electrodeposition from a cyanide bath, prepared by dissolving 1 g. of pure auric chloride in 6 times the quantity of potassium cyanide solution necessary for its conversion into the complex cyanide. The total volume was then made up to 500 c.c. The electrodeposition was carried out by a current of 20 mA per electrode for 3 min. on a platinum foil 1 × 1 cm. to give it a smooth coating. The current was then raised to 430 mA per electrode, and the electrodeposition continued for a further 10 min. to give a spongy deposit with a large surface. The electrodeposition was carried out between 55° and 60°. The prepared electrode was washed several times in conductivity water and then with the solution under investigation before it was introduced into the electrolytic cell. Each experiment was carried out with a freshly prepared electrode. The anode was placed in such a position with respect to the cathode as to ensure uniform distribution of the polarising current at the anode surface. The cathode was a platinum wire 2 cm. long and 0·1 cm. in diameter.

Measurements were carried out mainly in the following solutions: 0·1N-sulphuric acid, 0·2M-KH_2PO_4 + 0·2M-Na_2HPO_4 buffer mixture of approximate pH 6·8, 0·1M-sodium carbonate solution of pH 11·5, and 0·1N-sodium hydroxide, all prepared from " AnalaR " materials and conductivity water. The solution was boiled before use and cooled in an atmosphere of pure nitrogen to remove any dissolved oxygen.

The polarising currents used were 150 μA per electrode in sulphuric acid and phosphate buffer, and 10 and 300 μA in sodium carbonate solution and sodium hydroxide solution, respectively. In each solution three studies were carried out on each electrode—the anodic polarisation, the cathodic polarisation, and the anodic decay. The procedure adopted in obtaining the corresponding curves was as described before (El Wakkad and Emara, *J.*, 1952, 461). The reference half-cell was a saturated calomel electrode prepared as described before (*idem, loc. cit.*). The electrolytic cell and the reference half-cell were kept in an air thermostat at 25°±0·01°. The E.M.F. was measured with a Tinsley potentiometer and a mirror galvanometer. All potentials quoted are on the hydrogen scale.

Measurements of the Oxide Potentials of Gold.—The only oxide the existence of which has been completely established is Au_2O_3. On the other hand, preparation of Au_2O and AuO has often been claimed (Kruss, *Ber.*, 1886, **19**, 2541; *Annalen*, 1887, **237**, 241; Pollard, *J.*, 1926, 1347; Buchrer, Wartman, and Nugent, *J. Amer. Chem. Soc.*, 1927, **49**, 1271; Steigmann, *Chem.-Ztg.*, 1926, **50**, 595; Part, *Compt. rend.*, 1870, **70**, 842; Dudley, *Amer. Chem. J.*, 1902, **28**, 61; Schottlander, *Annalen*, 1883, **217**, 312; Gerke and Rouske, *J. Amer. Chem. Soc.*, 1927, **49**, 1855).

Owing to the extreme instability of aurous oxide, we intended to measure its potential at the moment of its formation against a gold electrode. A tall beaker of *ca.* 100 ml. capacity was fitted with a rubber bung having openings for a gold electrode, a syphon for the calomel electrode, inlet and outlet for nitrogen, and an opening for the nozzle of a burette. About 50 ml. of 0·01N-sodium hydroxide solution were placed in the beaker, boiled, and cooled in an atmosphere of pure nitrogen.

Aurous chloride, prepared by reduction of chloroauric acid with sulphurous acid (Pollard, *loc. cit.*), was allowed to drop from the burette. To ensure the absence of any oxide on the surface of the gold electrode, it was cathodically polarised and the current was interrupted directly before measurements.

For the preparation of the bivalent gold oxide we used the method of Kruss and Dudley (*locc. cit.*). Pure gold wire (0·88 g.) was dissolved in aqua regia, and the solution evaporated to dryness. A small amount of water was added and evaporated, and the process was carried out three times to eliminate nitric fumes. The crystals of gold chloride were taken up in the minimum amount of water, and auric oxide precipitated by addition of dilute sodium hydroxide at the b. p. of the solution, " AnalaR " sodium chloride being added to prevent formation of colloidal hydroxide. The oxide was dried and then heated at 160° in an air-oven to constant weight. The oxide potential measurements were carried out in 0·1N-sulphuric acid and in 0·1N-sodium hydroxide with a gold electrode.

Results and Discussion

Curves *A*, Figs. 1, 2, and 3, represent the characteristic anodic polarisation curves of gold at 25° in 0·1N-sulphuric acid, in phosphate buffer of pH 6·8, and in 0·1M-sodium carbonate solutions. The polarising currents were 150 μA per electrode in the first two

solutions and 10 μA per electrode in the last. From these curves, which show the variation of the potential of the gold electrode as it is forced from the hydrogen- to the oxygen-evolution potentials, it can be seen that there is a rapid initial build-up of potential which can be attributed—by analogy with the previous studies (El Wakkad and Emara, *loc. cit.*)—to the charging of the double layer. This is followed by three well-defined arrests before oxygen evolution. For the determination of the capacity of the double layer in this case, polarisation was carried out at extremely low current densities, *viz.*, 10 μA per electrode in both the sulphuric acid and the phosphate buffer, and 5 μA per electrode in the carbonate solution. Measurements from a large number of polarisation curves at such very low

FIG. 1.

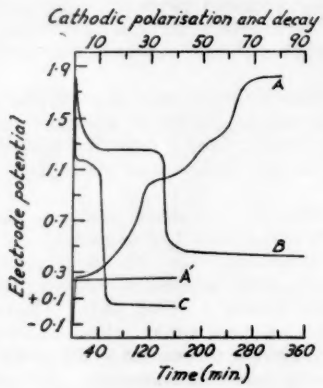


FIG. 2.

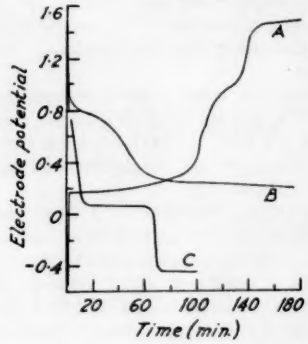


FIG. 3.

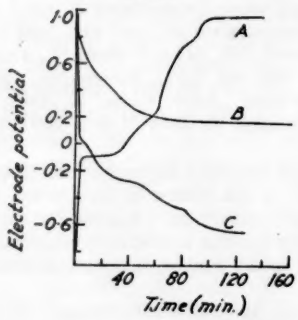
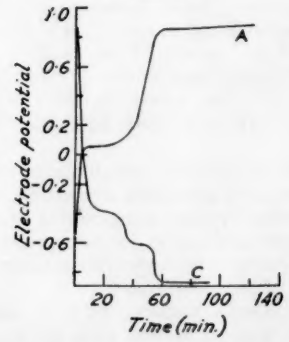


FIG. 4.



current densities gave an average value for the double layer capacity in 0·1N-sulphuric acid of about 2000 μF per electrode; in the phosphate buffer (pH 6·8) the average value was of the same order, but in 0·1M-sodium carbonate solution it was about 2500 μF per electrode.

The first step after the charging of the double layer appears to start at a potential of +0·27 v in 0·1N-sulphuric acid, and −0·05 and −0·25 v in the phosphate and carbonate solutions respectively. The last two values were obtained from charging curves carried out at extremely low current densities, *viz.*, 10 and 5 μA per electrode, for the determination of the capacity of the double layer as was stated before. The second step appeared to start at potentials of +0·96, +0·62, and +0·15 v in the three solutions respectively. The third step starts at potentials of +1·26, +0·86, and +0·70 v in the acid, neutral, and alkaline solutions, respectively.

Oxide Potentials of Gold.—In the Au–Au_2O system, the potential recorded within 20 sec. was −0·3 v, which changed towards a more positive value, becoming +0·60 v

after about 2 min. where it remained constant. The pH value of the hydroxide solution after the formation of the oxide was 12·0. If the potential recorded within the first 20 sec. is considered to represent a rather rough measure for the potential of the system $Au–Au_2O$, then $E°_B$ (the potential at the extreme alkaline range of pH) of the reaction $Au + 2OH^- = Au_2O + H_2O + 2e$ will be about −0·42 v. The rapid increase in the potential observed experimentally may be readily explained on the basis of the instability of the aurous oxide which decomposes rapidly into Au_2O_3 and gold. This is confirmed by the fact that the final potential recorded experimentally gives an $E°_H$ value (potential value at the extreme acid range of pH) for the system $Au–Au_2O_3$ of 1·32 v, in very good agreement with results obtained by Gerke and Rourke (*loc. cit.*), Buehrer and Roseveare (*J. Amer. Chem. Soc.*, 1927, **49**, 1989), and Hickling (*loc. cit.*).

In the Au–AuO system, a constant potential of +0·98 v was recorded in 0·1N-sulphuric acid from the beginning of the experiment and remained constant for over 6 hr. In 0·1N-sodium hydroxide solution the potential recorded was +0·27 v at first; it then drifted until it reached 0·41 v within one hour, where it remained constant.

In the following Table, the starting potentials of the three steps observed in the anodic polarisation curves are compared with the equilibrium potentials of the systems $Au–Au_2O$, Au–AuO, and $Au–Au_2O_3$ at the corresponding pH values.

	Starting potentials (v):			Equilibrium potentials (v) of the system:		
Solution	First step	Second step	Third step	$Au–Au_2O$	Au–AuO	$Au–Au_2O_3$
0·1N-H_2SO_4	+0·27	+0·96	+1·26	+0·36	+0·98	+1·30
Phosphate buffer ...	−0·05	+0·62	+0·86	0·00	+0·62	+0·94
0·1M-Na_2CO_3	−0·25	+0·15	+0·70	−0·24	(+0·38)	+0·70

The agreement between the starting potentials of these steps and the equilibrium values for the three systems (except for the value in parentheses, see p. 3102) strongly suggests that these three steps observed in the anodic polarisation curves correspond to the consecutive formation of Au_2O, AuO, and Au_2O_3 on the gold anode before evolution of oxygen.

The fact that in this case the agreement is between the starting potentials and the metal–metal oxide potentials and not between the oxidation–reduction potential of the higher and lower oxides as always found in previous studies (El Wakkad and Emara, *locc.cit.*) can be explained by the instability of the lower oxides, for it is well known that Au_2O and AuO are unstable in aqueous solutions (Pollard, *loc. cit.*; Jirsa and Buryanek, *loc. cit.*), decomposing to Au_2O_3 and gold.

The instability of the aurous ion in aqueous solutions is also obvious from the fact that the standard potentials of the systems $Au \longrightarrow Au^+ + e$ and $Au \longrightarrow Au^{3+} + 3e$ are *ca.* 1·68 v and *ca.* 1·42 v, respectively (Latimer, "The Oxidation States of the Elements and their Potentials in Aqueous Solutions," New York, 1938, p. 182), which shows that the potential of the $Au–Au^+$ system is more positive than that of the $Au–Au^{3+}$ system, indicating the instability of the former.

The quantity of electricity passed in the first step in the case of the carbonate solution was about 15,000 μC. This is sufficient for the liberation of about $4·65 \times 10^{16}$ oxygen atoms. The specific gravity of gold being taken as 19·3, the diameter of the gold atom may be calculated as $2·6 \times 10^{-8}$ cm., and hence there would be about $1·5 \times 10^{15}$ atoms of gold per true sq. cm. A rather rough estimate for the ratio of the real to the apparent area of our gold electrode may be obtained from the capacity of the double layer. The capacity of the anodic double layer before oxide formation as obtained from previous studies (El Wakkad and Emara, *loc. cit.*) can be estimated as 100 μF per true sq. cm. If the difference between the capacity of our gold electrode and that for the true sq. cm. is assumed to be due only to the difference in the surface area, the ratio of the real to the apparent area will be about 12·5, and the true surface area of our gold electrode will be about 25 sq. cm. This value gives about $3·75 \times 10^{16}$ gold atoms on the surface of our electrode. This shows that the quantity of electricity passed in the first step corresponds to the formation of an Au_2O film about 2 molecules thick. It must be emphasised that these results are very approximate owing to the instability of this oxide in aqueous solutions, as was shown before. The quantity of electricity passed in the second step was about 15,000 μC per

electrode, suggesting that the film of AuO is also about 2 molecules thick, and similarly from the third step it appears that the film of AuO was further oxidised to Au_2O_3, *i.e.*, the film of Au_2O_3 is also about 2 molecules thick. These results for the thickness of Au_2O_3 on the gold anode before oxygen evolution are in agreement with those obtained by Shutt and Walton (*loc. cit.*).

In 0·1N-sulphuric acid solution, the quantity of electricity passed in the first step was about 315,000 μC, *i.e.*, sufficient for the liberation of $9{\cdot}76 \times 10^{17}$ atoms of oxygen. The ratio of the real to the apparent area being taken as 10 (from capacity measurements), there will be 3×10^{16} gold atoms on our electrode. This result indicates that the oxide film in this case is 32 molecules thick. This very high value suggests that the oxide in such solution is somewhat more soluble than in the carbonate solution. In order to test this assumption, the behaviour of the gold anode in 9N-sulphuric acid was studied. The result, shown in curve *A'*, Fig. 1, indicates that when the gold anode was polarised in such a strong acid solution, the potential did not rise to the oxygen-evolution value but remained constant at the Au–Au_2O potential, thus confirming our view. From this behaviour, the standard condition ought to be that of the carbonate solution.

The behaviour of gold in 0·1N-sodium hydroxide solution, Fig. 4, is somewhat different from that in all the other solutions, for in this case one step was recorded, which began at about −0·2 v when an extremely low polarising current (10 μA per electrode) was used, and at about +0·00 v at 300 μA per electrode before oxygen evolution.

This anomalous behaviour of gold in such alkaline solutions was noticed also by most of the previous authors (Armstrong, Himsworth, and Butler; Hickling, *locc. cit.*), and it seems to be due to the amphoteric character of the gold oxides which form aurite and aurate in such strong alkaline solutions. This fact may explain also the difference between the potential of the second step in the carbonate solution and that for the Au–AuO system.

The cathodic curves *C*, Figs. 1—3, show reduction steps at the Au_2O_3 potential at the corresponding pH values, and another step at the Au–Au_2O potential before hydrogen evolution. The existence of the first step is in accordance with the fact that Au_2O_3 was formed on the electrode during the anodic polarisation. The presence of the second step is unexpected owing to the instability of aurous oxide as was shown before. Hickling (*loc. cit.*) observed the same step during his oscillographic study of the gold electrode. Several experiments on the cathodic polarisation of the gold anodes showed that this step always appeared in the neutral and the carbonate solutions, whereas in acid solutions its appearance depended upon the experimental conditions such as the polarising current density during the anodic polarisation and the duration of the anodic polarisation at the oxygen-evolution potential. These facts seem to indicate, as suggested by Hickling (*loc. cit.*), that this arrest observed during the cathodic polarisation was due to oxygen in the solution formed during the anodic polarisation. As will be seen from the discussion of the decay curves, the oxygen may originate also from the decomposition of Au_2O_3. As this step always takes place at the Au–Au_2O potential at the corresponding pH values, it seems that the oxygen reacts first with the gold to give Au_2O, which is then reduced by cathodic current to the metal before hydrogen evolution. There is no step corresponding to the reduction of the AuO oxide in any of the solutions.

The decay curves *B*, Figs. 1—3, show a step at the potential of Au_2O_3 at the corresponding pH values, after which the potential of the gold electrode fell to a value slightly more positive than that of the Au–Au_2O system. There is no step corresponding to the decomposition of AuO. These results suggest that the higher oxide Au_2O_3 is unstable in contact with the metal, which is in accordance with the previous findings in all the metals studied (El Wakkad and Emara, *loc. cit.*; Tourky and El Wakkad, *J.*, 1948, 740, 749; El Wakkad, *J.*, 1950, 3563). The fact that the potential became constant at a value more positive than that of the Au–Au_2O system is quite in harmony with the fact that Au_2O is unstable, decomposing to gold and Au_2O_3, and since the latter is also unstable in contact with the metal, one must expect that the potential of the electrode will be intermediate between the values of the systems Au–Au_2O and Au–Au_2O_3 as found experimentally.

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The Anodic Oxidation of Metals at Very Low Current Density. Part VI. Tin.*

By S. E. S. El Wakkad, A. M. Shams El Din, and (Miss) Jeannette A. El Sayed.

[Reprint Order No. 5124.]

The anodic oxidation of tin at very low current density is examined in solutions of different pH values. It is shown that in weakly alkaline electrolytes the tin anode becomes passive. The initial stage in this process is the formation of a layer 1—2 molecules thick of stannous hydroxide on the electrode surface which is further oxidised to stannic hydroxide before evolution of oxygen. In strongly alkaline, neutral, and acid solutions no passivation occurs at such very low current densities. In nitric acid solutions two types of passivity, chemical and electrochemical, are found to take place.

In continuation of previous work (El Wakkad and Emara, *J.*, 1952, 461; 1953, 3504, 3508), the anodic oxidation of tin at very low current density has been investigated. No previous work on tin from the present standpoint has been published but other methods of investigation have yielded some indirect although somewhat conflicting information; thus Schon (*Z. anal. Chem.*, 1871, **10**, 291) showed that tin becomes passive in nitric acid when in contact with platinum. Foerster and Dolch (*Z. Elektrochem.*, 1909, **16**, 559) found that tin anodes passed into sodium hydroxide solutions as bivalent ions until a definite concentration was attained and then the potential changed almost instantaneously to a more positive value and the dissolved tin was oxidised to the quadrivalent state and oxygen was liberated at the anode, which had become passive. Valessi (*Boll. Soc. Eustachiana*, 1933, **31**; *Chem. Zentr.*, 1933, II, 2318), on the other hand, found that tin anodes in sodium hydroxide solutions dissolved directly as sodium stannite and sodium stannate. Newbery (*J.*, 1916, 1066) found that tin showed no passivity in acid electrolytes but readily became passive in alkaline solutions, and Rothmund (*Z. physikal. Chem.*, 1924, **110**, 384) and Steinherz (*Z. Elektrochem.*, 1924, **30**, 279) found that tin could be made passive in sulphuric, hydrochloric, hydriodic, hydrobromic, and hydrofluoric but not in nitric, iodic, perchloric, and acetic acids. Knowlton (*J. Phys. Chem.*, 1928, **32**, 1572) considered the passivation of tin in nitric acid to be due to formation of oxide film and not to that of stannic nitrate. Kerr (*J. Soc. Chem. Ind.*, 1938, **57**, 405) studied the anodic films formed on tin in sodium hydroxide solution. He found that at lower temperatures a brown film was formed, whereas at higher temperatures a yellow film was obtained. Analysis of the brown film gave SnO_2, 80·9; SnO, 9·3; H_2O, 9·8%, and that of the yellow film gave SnO_2, 68·5; SnO, 12·4; H_2O, 19·1%. Bianchi (*Chimica e l'Industria*, 1947, **29**, 295) studied the anodic passivation of tin in alkaline solutions and three different types of films were noticed on the passive metal; this colour varied from dark to light brown depending on the current density used.

The results of investigations on the nature of films formed on metallic tin, when exposed to or heated in air or oxygen, seem to indicate that on the surface of the metal stannous oxide is first formed, then stannic oxide (Steinheil, *Ann. Physik*, 1934, **19**, 465).

In the present study it is shown that in weakly alkaline electrolytes tin anodes at very low current densities become passive. The initial stage in this process is the formation of a layer 1—2 molecules thick of $Sn(OH)_2$ on the electrode surface, and this is further oxidised to $Sn(OH)_4$ before evolution of oxygen. In strongly alkaline, neutral, and acid solutions no passivation occurs at such very low current densities. In nitric acid solutions two types of passivity take place, chemical and electrochemical.

Experimental

The electrical circuit and the electrolytic cell used were as previously described (El Wakkad and Emara, *J.*, 1952, 461). The tin anodes were prepared by electrodeposition from a bath prepared by dissolving 2·8 g. of $SnCl_2,2H_2O$ in 40 ml. of 2N-sodium hydroxide. Deposition

* Part V, preceding paper.

was carried out at a current of 15 mA/electrode for 20 min. at 80° on a platinum foil of 1 cm.^{2} apparent area. The deposited tin was in a spongy form, so direct measurement on the variation of its potential when polarising it anodically at very low current density was possible. The tin electrode was washed several times with conductivity water, and then with the solution in which it was to be studied before it was introduced into its compartment in the electrolytic cell. Each experiment was carried out with a freshly prepared electrode from a fresh bath. The anode was placed in such a position with respect to the cathode as to ensure uniform distribution of the polarising current at the anode surface. The cathode was a platinum spiral about 10 cm. long and 0·1 cm. in diameter.

Measurements have been carried out mainly in 0·1M-sodium borate (pH 9·2) with use of a polarising current of 20 μA/electrode, in 0·1M-sodium carbonate solution (pH 11·5) with a polarising current of 200 μA/electrode, in 0·1N-sodium hydroxide (pH 13), in the phosphate–citric acid neutral buffer solution of pH 7, in 0·1M-sodium sulphate solution of pH 7, and in 0·1N-hydrochloric acid (pH 1). In the last four solutions the polarising currents used were 200—400 μA per electrode. The behaviour of the tin anode in 0·1N-nitric acid was also studied by use of a polarising current of 400 μA/electrode. The solution in the cell was boiled before use and cooled in an atmosphere of pure nitrogen to remove dissolved oxygen. The detailed experimental procedure for obtaining the anodic, the cathodic, and the decay curves was essentially as described before (El Wakkad and Emara, *loc. cit.*). In the case of nitric acid solution two procedures were adopted in obtaining the anodic curves; the first was the usual one, and in the second the tin electrode was immersed under cathodic current, *i.e.*, the current was switched cathodically on the electrode before dipping it in the solution. The polarising current was then reversed to start the anodic polarisation.

Results and Discussion

Curve *A*, Fig. 1, is the characteristic anodic polarisation curve of tin at 25° with a polarising current of 200 μA in 0·1M-sodium carbonate. Curve *A*, Fig. 2, is the same anodic polarisation curve in sodium borate solution of pH 9·2 for a polarising current of 20 μA. From these curves, which show the variation of the potential of the tin anode with the quantity of electricity passed, it can be seen that, at first, there is a rapid initial build-up of potential, ascribed, by analogy with the cases previously studied (El Wakkad and Emara, *locc. cit.*), to the charging of the double layer which is followed by two well-defined arrests before oxygen evolution. Measurements from a large number of polarisation curves gave an average value for the double-layer capacity of ~1600 μF/electrode for the tin anode under investigation in the carbonate solution of pH 11·5. In the borate solution of pH 9·2, the average value was ~6700 μF/electrode.

The standard condition was taken to be the borate solution since in this solution the oxides of tin possess minimum solubilities. The first arrest after the charging of the double layer appears to start at −0·74 v in sodium carbonate solution and at −0·61 v in the borate solution. The second arrest appears to start at −0·62 and −0·53 v in the two solutions respectively.

In the following table are shown the starting potentials of these two arrests in the two electrolytes as compared with the equilibrium potentials of the systems Sn–$Sn(OH)_2$ and $Sn(OH)_2$–$Sn(OH)_4$ at the corresponding pH values. These equilibrium potentials were obtained as follows: The free energies of stannous hydroxide, stannic hydroxide, and hydroxyl ions being taken as −115,200, −226,000, and −37,585 cal., respectively (Latimer, "The Oxidation States of Elements and their Potentials in Aqueous Solutions," New York, 1938, p. 137), the free-energy changes of the reactions

$$Sn + 2OH^- = Sn(OH)_2 + 2e;\ \Delta F = -40{,}030 \text{ cal.}$$

and

$$Sn(OH)_2 + 2OH^- = Sn(OH)_4 + 2e;\ \Delta F = -35{,}630 \text{ cal.}$$

give $E_B°$ (the potential value at the extreme alkaline range of pH) as −0·87 v and −0·77 v for the two systems, respectively.

By applying the ordinary equation for the variation of the potential of these systems with pH, the values shown in cols. 4 and 5 in the following table were obtained. The

very close agreement between the first and the second arrests and the equilibrium values for the two systems leaves little doubt that these two steps in the anodic polarisation in such solutions correspond to the consecutive formation of stannous hydroxide or oxide and stannic hydroxide or oxide on the tin anode before evolution of oxygen.

Solution	Starting potential of the first arrest, v	Starting potential of the second arrest, v	Equilibrium potential of the system $Sn–Sn(OH)_2$, v	Equilibrium potential of the system $Sn(OH)_2–Sn(OH)_4$, v
0·1M-Carbonate	−0·74	−0·62	−0·72	−0·62
0·1M-Borate ...	−0·61	−0·53	−0·58	−0·48

The quantity of electricity passed from the beginning to the end of the first step in the borate solution was found to be about 30,000 μc/electrode. This is sufficient for the liber-

FIG. 1.

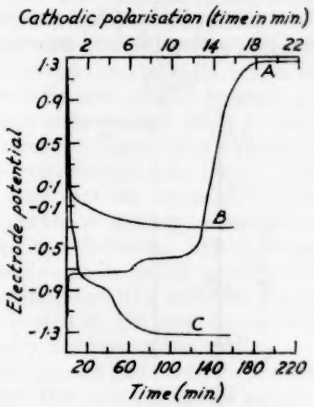


FIG. 2.

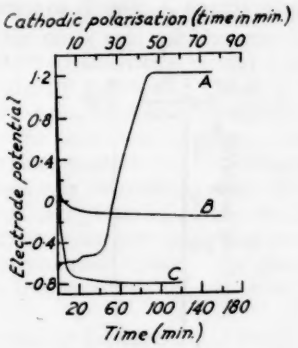
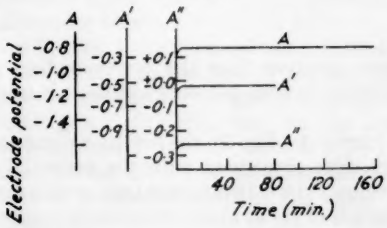


FIG. 3.



ation of about $9·42 \times 10^{16}$ atoms of oxygen. The diameter of the tin atom being taken as $3·04 \times 10^{-8}$ cm. (from specific gravity), there would be about $1·08 \times 10^{15}$ atoms of tin per true sq. cm. at the tin surface. A rather rough estimate for the ratio of the real to the apparent area of the tin anode under investigation can be obtained from the value of the capacity of the double layer at the anode under the standard conditions and comparison of this with the capacity of the real area which is estimated from previous studies as 100 μF/true sq. cm. (El Wakkad and Emara, *locc. cit.*). This gives the value of 67 : 1 for the ratio real : apparent area of our tin anode, and hence there would be about $7·24 \times 10^{16}$ atoms of tin on the whole surface of our electrode. This shows that the quantity of electricity passed in the first step corresponds to the formation of a stannous hydroxide film 1—2 molecules thick.

The quantity of electricity passed in the second step is of the same order as that of the first step, suggesting the conversion of stannous hydroxide or oxide into stannic hydroxide or oxide.

In 0·1N-sodium hydroxide solution, curve *A*, Fig. 3, the result indicates anodic dissolution at −0·84 v. This is in very close agreement with the potential of the system Sn–$Sn(OH)_2$ at the corresponding pH value, *viz.*, −0·81 v, which suggests that the anodically formed stannous hydroxide is freely soluble in the alkaline hydroxide.

Calculation of the standard potentials of the systems Sn–$Sn(OH)_6^{--}$ and Sn–$HSnO_2^-$ gives the following interesting results:

The free energies of $Sn(OH)_6^{--}$, $HSnO_2^-$, water, and hydroxyl ion being taken as −306,000, −92,450, −56,690, and −37,575 cal., respectively (Latimer, *op. cit.*), the free-energy changes of the reactions are

$$Sn + 6OH^- = Sn(OH)_6^{--} + 2e;\ \Delta F = -80{,}490 \text{ cal., and hence } E_B^\circ = -1{\cdot}74 \text{ v}$$

and

$$Sn + 3OH^- = HSnO_2^- + H_2O + 2e;\ \Delta F = -36{,}385 \text{ cal., and hence } E_B^\circ = -0{\cdot}79 \text{ v}$$

This suggests that, although in alkaline solutions the stannous hydroxide is expected to be freely soluble (curve *A*, Fig. 3) to form the stannite, yet as the standard potential of the

FIG. 4.

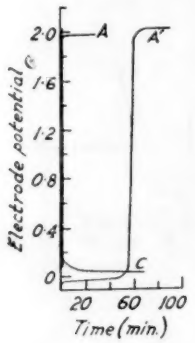
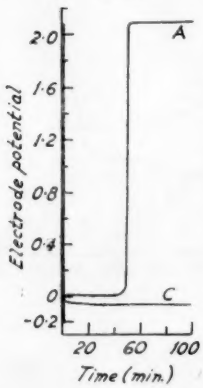


FIG. 5.



system tin–stannite is more positive than the corresponding potential of tin–stannate, one must expect that the former in such alkaline solutions is unstable, decomposing to the stannate.

For solutions of pH 7 (curve *A'*, Fig. 3), the results indicate anodic dissolution of tin at −0·45 v, which is in very close agreement with the potential of the system Sn–$Sn(OH)_2$ at the corresponding pH value. In 0·1N-hydrochloric acid (curve *A''*, Fig. 3), the results also indicate anodic dissolution of tin at about its reversible potential.

The passivation of tin in 0·1N-nitric acid solution is of great interest. Curves *A* and *A'*, Fig. 4, show the characteristic anodic polarisation curves of tin in such a solution with a current of 400 μA/electrode. Curve *A* was obtained by the usual procedure, but curve *A'* was obtained by the modified procedure in which the current was switched on cathodically before the tin electrode was dipped into the nitric acid solution. From curve *A*, Fig. 4, it can be seen that the potential of the electrode jumped directly from the hydrogen- to the oxygen-evolution values as soon as the anodic polarisation started. This indicates that in the usual procedure the tin electrode became passive as soon as it was dipped in the nitric acid solution; the cathodic treatment was not able to activate the electrode, and thus when the polarising current was reversed to start the anodic polarisation the potential of the anode jumped directly to the oxygen-evolution value. Further evidence for this view comes from the fact that the constant potential registered when the electrode was polarised cathodically before starting the anodic polarisation under these conditions coincided with the potential of the system Sn–$Sn(OH)_2$ at the corresponding pH value.

With the modified procedure, although the constant potential registered when the elec-

trode was polarised cathodically was found to coincide also with the $Sn–Sn(OH)_2$ potential at the corresponding pH value, yet when the polarising current was reversed anodically, the potential of the electrode did not jump directly to the oxygen-evolution value, but a well-defined step appeared, indicating oxide formation. This step started at a potential approaching that of the system $Sn(OH)_2–Sn(OH)_4$, where it remained for a comparatively long time, after which the potential changed to the oxygen-evolution value. These results indicate two types of passivity: chemical passivity by the action of nitric acid, and electrochemical passivity by the anodic current. When the tin electrode was dipped in the nitric acid solution it became passive by chemical means; the cathodic polarisation of the electrode was then unable to reduce the oxide formed, since the rate of reduction was less than the rate of oxidation. When the polarising current was reversed anodically, the potential of the electrode jumped directly to the oxygen-evolution value. On the other hand when the current was switched on to the electrode cathodically before dipping it in the nitric acid solution, the chemical passivity was greatly reduced and a definite step appeared on the anodic polarisation.

One must expect that, if this is the case, when a higher polarising current is switched on to the electrode cathodically before dipping it in the nitric acid solution, the chemical passivity will be still greatly reduced and the quantity of electricity passed during the anodic polarisation for the oxide formation will be greatly increased. Curve *A*, Fig. 5, shows the result obtained when a polarising current of 1·5 mA/electrode was switched on to the tin electrode cathodically before it was dipped in the nitric acid solution. From this curve it is clear that the tin-cathode potential is then more negative than in the other two cases. When the polarising current of 1·5 mA/electrode was reversed to start the anodic polarisation, a well-defined step appeared, starting at the potential of the system $Sn–Sn(OH)_2$, and changed rather quickly with such comparatively high polarising current to that of $Sn(OH)_2–Sn(OH)_4$ before rising to the oxygen-evolution value. The quantity of electricity passed in the step of oxide formation is comparatively greater than in the previous cases, confirming our view.

The anodic decay (curves *B*, Figs. 1 and 2) reveals that, on interruption of the polarising current when the anode is at the oxygen-evolution potential, the potential dropped to a value somewhat more positive than the corresponding value of the sytem $Sn(OH)_2–Sn(OH)_4$, and then changed—although very slowly—towards the potential of the above system. This is reached after a period varying between 18 and 24 hr.

The cathodic curves (curves *C*, Figs. 1 and 2) reveal the reduction of stannic and stannous hydroxides before hydrogen evolution. In the case of sodium carbonate solution, curve *C*, Fig. 1, the two reduction steps are quite clear and started at the reversible potentials of the systems $Sn(OH)_4–Sn(OH)_2$ and $Sn(OH)_2–Sn$. In the borax solution, curve *C*, Fig. 2, the reduction steps were less clear.

The cathodic curves obtained for the nitric acid solution, curves *C*, Figs. 4 and 5, show that the potential of the electrode dropped directly to the value of the system $Sn(OH)_2–Sn(OH)_4$, where it remained constant.

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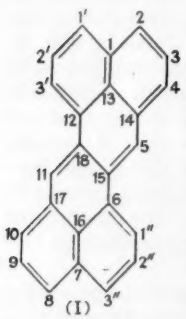
Molecular-orbital Calculations for Clar's Hydrocarbon 1 : 13 : 12-6 : 16 : 7-*Dibenzonaphthacene* (*Zethrene*). *Part II*. The Diels–Alder Reaction.*

By C. A. Coulson, Carl M. Moser, and Michael P. Barnett.

[Reprint Order No. 5204.]

Molecular-orbital calculations for all the geometrically possible positions of attack in the Diels–Alder reaction of the polynuclear hydrocarbon 1 : 13 : 12-6 : 16 : 7-dibenzonaphthacene (Clar's zethrene) with maleic anhydride suggest that the reaction should proceed much more favourably for one pair of positions (1″ : 5 and 11 : 3′) than for any other position. This prediction, which has not yet been tested experimentally, correlates well with the free-valence data for this hydrocarbon.

We have recently discussed certain properties of the polynuclear hydrocarbon 1 : 13 : 12-6 : 16 : 7-dibenzonaphthacene (" zethrene "; I) using the simple molecular-orbital method (Coulson and Moser, *J.*, 1953, 1341). Now zethrene belongs to the class of condensed hydrocarbons which readily undergo Diels–Alder addition of maleic anhydride; it is known (see later) that this reaction does occur with zethrene, but the location of the points of attack are not known and it would be a problem of some considerable difficulty to characterise the positions in the molecule across which the addition takes place. This is a situation in which theoretical prediction may well prove exceedingly valuable; it is the object of this communication to report such predictions. For this purpose we use the theory originally proposed by R. D. Brown (*J.*, 1950, 691, 2730; 1951, 1612, 3129) to account for the Diels–Alder reaction between dienes and dienophiles. The formation of an adduct in this reaction, as, *e.g.*, between $C_{(2)}$ and $C_{(14)}$, or $C_{(5)}$ and $C_{(1'')}$, involves the removal from the resonating framework of the two centres at which addition occurs, and also the removal of two of the π-electrons. These are needed in the formation of the two new C–C bonds. It is convenient mathematically to regard this process as being achieved in two stages: (*a*) we localise two π-electrons on the appropriate atoms of the dienophile and thus remove these atoms from the conjugation path; (*b*) we subsequently use these two localised electrons to form the new bonds to the diene. The fundamental assumption of Brown's theory is that the relative ease of formation of the adduct at atoms m and n of the hydrocarbon, depends only on the energy required in stage (*a*), provided of course that m and n are of proper geometrical orientation for the reaction to take place. In the case of polynuclear hydrocarbons this condition is taken to imply that m and n are *para* to one another in the conjugated hydrocarbon. The para-localisation energy P which is thus involved, is defined by



(I)

$$P = E_r - E + 2\alpha \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

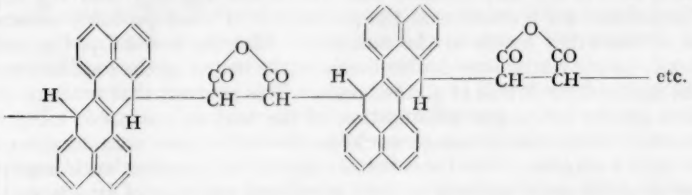
where E is the π-electron energy of the original conjugated system, 2α is the energy of two isolated π-electrons (α is generally taken to be the arbitrary zero of the energy scale for each electron, in calculations of this kind), and E_r is the total π-electron energy of the " residual molecule." This " residual molecule " consists of the one or more separate conjugated systems left when the two carbon atoms m and n are isolated. Our object therefore is to calculate the localisation energy P. A comparison of P for different possible positions should show at once which is the most likely one for the reaction.

To calculate P we need E and E_r. In the simplest M.O. theory these are expressed in terms of the resonance integral β, where, in usual notation $\beta = \int \phi_i^* H \phi_j d\tau$, and all overlap integrals such as S ($\equiv \int \phi_i \phi_j d\tau$) are neglected. A better approximation includes S, and then computes E and E_r in terms of a new resonance integral γ, where $\gamma = \beta - S\alpha$. In the present work there is a particular reason for preferring the second approximation, for although the amount of quantitative experimental data reported in the literature for the

* The paper, *J.*, 1953, 1341, is considered as Part I.

Diels–Alder reaction is not extensive, the agreement between theory and experiment for certain derivatives of benzanthracene (Bachmann and Kloetzel, *J. Amer. Chem. Soc.*, 1938, **60**, 481) is almost quantitative when the energies are expressed in terms of γ, but only qualitative when in terms of β. In order to make these calculations at all simply, it was necessary to extend certain previous formulæ introduced by Coulson (*Proc. Camb. Phil. Soc.*, 1940, **36**, 201) and de Heer (*Phil. Mag.*, 1950, **41**, 370). In view of the wider application of these new formulæ, we have put them in the separate, following paper. We have taken S to be uniformly 0·25 for neighbouring atoms, and otherwise zero.

Clar and his collaborators have shown that the reaction takes place quite readily with zethrene; for the green colour of the solution of zethrene is rapidly discharged. But no information is available by this means about the structure of the adduct. There are in the main two possibilities, either that the adduct is a simple one-to-one complex as in other molecules so far studied, or, as was suggested to us by a referee, that it is a copolymer such as



We have only considered the first of these possibilities, despite the attractive nature of the second which allows zethrene to be attacked at its most reactive positions. This is because Dr. Clar, to whom we are much indebted for information about this reaction, tells us that he has so far found no evidence to suggest a polymer formation, and also the type of attack which we shall later be led to suggest is one already familiar in certain other reactions, in particular with perylene. We have therefore thought it worth while (*a*) to show by comparison of the localisation energy P for zethrene and other hydrocarbons that the reaction would be expected on theoretical grounds, and (*b*) to predict the structure of the adduct by a comparison of the P-values for all of the ten geometrically plausible positions. Our conclusion in both (*a*) and (*b*) is quite unambiguous.

The results of our calculations are shown in the Table. It is unnecessary to give many details of the technique used, since this is either quite standard, or else follows directly the procedure recommended in the paper which follows. A few comments, however, are reserved for the appendix. Columns 1 and 5 give the positions at which the addition is geometrically possible. These are arranged in such a manner that the sequence of P-values, shown in columns 2 and 6 in γ-units, is an increasing one. This means that the most likely positions are those at the top left, and the least likely are those at the bottom right. Columns

Diels–Alder reaction with zethrene.

Positions	$P(\gamma)$	$P(\beta)$	Sum of free valences	Positions	$P(\gamma)$	$P(\beta)$	Sum of free valences
1″ : 5	2·33	3·59	0·359	1″ : 7	3·48	4·56	0·251
3″ : 6	2·85	4·21	0·299	2″ : 16	3·58	4·61	0·231
8 : 17	3·00	4·29	0·278	9 : 16	3·68	4·64	0·230
7 : 10	3·43	4·53	0·270	16 : 18	4·10	5·01	0·305
6 : 11	3·47	4·40	0·349	15 : 17	4·29	5·36	0·258

3 and 7 show P-values in β-units, and columns 4 and 8 give the sum of the corresponding free valences calculated from our previous molecular diagram for this molecule.

An inspection of this Table shows that the position 1″ : 5 (or the equivalent 3′ : 11) is very considerably favoured. Since the difference in P-values appears as an exponent in the rate of reaction, this suggests very strongly that these are the positions of the adduct. Fortunately the same conclusion is reached even when P is expressed, by using the simpler theory, in terms of β instead of γ, and also when the sum of the appropriate free valences is used as criterion instead of localisation energies. Now there are reasons for believing that

the free-valence values will control the early stage of such a reaction as this, and the localisation energy the later (*i.e.*, transition) stage. The complete agreement between the results of columns 2, 3, and 4 gives strong support to the correctness of the conclusion. (The sequence of P-values is almost unchanged in passing from the γ-scheme to the β-scheme, there being only one quite minor inversion. But the correlation with free valences, while still good, is nothing like so perfect.)

Quantitatively the value $2{\cdot}33\,\gamma$ (or $3{\cdot}59\,\beta$) does not indicate an exceedingly fast reaction. Brown has used the 9 : 10-positions of anthracene (the *meso*-positions), where $P = 3{\cdot}31\,\beta$, as a standard reaction rate, with respect to which other rates may be compared. On this basis the reaction would be expected to occur, but would only be about 10^{-6} as rapid as in anthracene. We are inclined to believe that this is not a very serious discrepancy: for in calculating E and E_r we have adopted the usual assumption of simple molecular-orbital theory, that all the β's and γ's are equal. Now our predictions of bond lengths (Table 2, Coulson and Moser, *loc. cit.*) indicate that the bonds $C_{(5)}$–$C_{(15)}$ and $C_{(6)}$–$C_{(1'')}$, both of primary importance for a reaction at the positions 5 : 1'', are probably somewhat shorter than most of the other bonds in the molecule. Also the bonds $C_{(1')}$–$C_{(2')}$ and $C_{(2'')}$–$C_{(3'')}$, which have to be converted into double bonds in the course of the localisation process, are already the most nearly double of all the bonds. This suggests that we could get improved quantitative results by proper modification of the various resonance integrals for these various bonds. Only a small change would be needed to cause considerable change in the predicted rate of reaction. We have not attempted to introduce such improvements because they would be most unlikely to alter calculated positions of attack, and better comparison with other values for different molecules reported in the literature is obtained if we keep to the standard resonance integrals. To make such changes is perfectly possible, but very laborious.

In all other polynuclear hydrocarbons so far investigated, Brown has found the reactive positions for Diels–Alder reaction to be the *meso*-positions of the anthracene-like part of the conjugated molecule. This is apparently not a general rule, for in zethrene the corresponding positions are 11 : 6 (or 5 : 12), and our calculations predict them to be fifth in order of decreasing probability. (But the free-valence criterion would make them second.)

Notes on the numerical calculations

In principle, the calculation of E_r presents no unusual difficulties, but in practice it is distinctly tedious to have to find all the roots of ten or more polynomials of the 22nd degree, with the aid of nothing more than a desk machine. Furthermore only the total energy, and not the individual energy values, was needed. For that reason we used formula (16) of the following paper. This expresses the energy E of any conjugated hydrocarbon in the form

$$E = \frac{2\sqrt{(Nn)}\gamma}{1 + Sx} + \frac{2\gamma}{\pi}\int_0^\infty \frac{1 - S^2t^2}{(1 + S^2t^2)^2} \ln \frac{\Delta(it)}{(t^2 + x^2)^n}\,\mathrm{d}t,$$

where N = number of carbon–carbon bonds in the molecule, $2n$ = number of π-electrons in the system, $\Delta(\varepsilon)$ = secular determinant as a function of the energy ε, $x^2 = N/n$, $t = \varepsilon/\beta$, and $i^2 = -1$.

We first expanded the polynomials $\Delta(\varepsilon)$ for each of our ten residual molecules, and then evaluated them numerically from $k = 0$ to $k = 6$ at suitable intervals, using an I.B.M. punched-card machine model 602A. We used a floating-decimal scheme devised by one of us (M. P. B.). The remainder of the computation, which involved numerical integration from 0 to 6, a ten-strip formula from 9 to 2 and 2 to 6, and an asymptotic expression for the contribution to the integral from $t > 6$ being used, was carried through on a desk machine. We acknowledge the facilities for the earlier part of these calculations which were provided by the I.B.M. Company in London. We believe that our values for P in the Table are accurate to about 1 or 2 in the second decimal place.

One of us (M. P. B.) thanks the Board of the British Rayon Research Association for a Fellowship during the tenure of which this work was carried out.

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The Calculation of Resonance and Localisation Energies in Aromatic Molecules.

By C. A. Coulson.

[Reprint Order No. 5203.]

A simple method is described whereby the π-electron resonance energy of an aromatic or conjugated molecule, and the localisation energies required in the discussion of chemical reactivity, may be obtained by means of one single numerical integration, without the need for explicit calculation of any of the energies of the separate molecular orbitals. The overlap integral may be included in these calculations.

It is often desired to calculate the resonance energy, or one of the possible localisation energies, for the π-electrons in an aromatic or conjugated molecule. For example, Coulson, Moser, and Barnett (preceding paper) required the para-localisation energy for various possible positions of reaction between maleic anhydride and Clar's six-ringed polynuclear hydrocarbon 1 : 13 : 12-6 : 16 : 7-dibenzonaphthacene (zethrene). One way of making all these calculations is by direct solution of the appropriate secular determinants to give the energies of all the allowed molecular orbitals. But this is tedious, and may be avoided in the following manner. First, let us consider alternant hydrocarbons, since these are at present by far the best understood.

If we make the usual assumptions of simple molecular-orbital theory, that (i) all Coulomb terms have the same value α, (ii) all resonance integrals between neighbours have the same value β, (iii) all other resonance integrals are zero, and (iv) all overlap integrals between adjacent atomic orbitals have the same value S, and all other overlap integrals are zero, then, as Wheland (*J. Amer. Chem. Soc.*, 1941, **63**, 2025) and others have shown, the energies of the allowed molecular orbitals take the form

$$\varepsilon_j = \alpha + m_j\gamma \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where

$$\gamma = \beta - \alpha S \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and m_j, which varies from one level to another, is related to the corresponding energy $(\alpha + k_j\beta)$ obtained with neglect of overlap, by the equation

$$m_j = k_j/(1 + k_jS) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

It is convenient to measure energy from a zero corresponding to $\varepsilon = \alpha$. This means that the term α in (1) may be omitted, so that $\varepsilon_j = m_j\gamma$.

The ε_j are found as roots of the secular determinant, and $z = k_j\beta$ is a root of the equation

$$\Delta(z) = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where $\Delta(\varepsilon)$ is the familiar secular determinant without overlap integrals. In general β and γ are both negative, and all the levels for which $k_j > 0$ (and therefore also $m_j > 0$) are doubly filled. Those for which $k_j < 0$ are empty. There may or may not be certain zero-energy orbitals, and these may have 0, 1, or 2 electrons in them. But their presence makes no difference to the total π-electron energy E which, by the method introduced by the author (*Proc. Camb. Phil. Soc.*, 1940, **36**, 201), may be expressed as a contour integral :

$$E = \frac{\gamma}{\pi i}\oint \frac{z}{\beta + Sz}\frac{\Delta'(z)}{\Delta(z)}\,\mathrm{d}z \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

In this integral, which is valid for the case where $S = 0$ as well as $S \neq 0$, Δ' denotes $\mathrm{d}\Delta/\mathrm{d}z$ and the contour consists of the complete imaginary axis and the infinite semicircle

to its left. For an alternant hydrocarbon $\Delta'(z)/\Delta(z)$ is an odd function of z so that, as de Heer (*Phil. Mag.*, 1950, **41**, 370) shows, (5) may be written as

$$E = \frac{\beta\gamma}{\pi i}\oint \frac{z}{\beta^2 - S^2z^2}\frac{\Delta'(z)}{\Delta(z)}\,dz = \frac{\beta\gamma}{\pi i}\oint \frac{z}{\beta^2 - S^2z^2}\frac{d}{dz}\log\,\Delta(z)\,dz \quad . \quad . \quad . \quad (6)$$

Now let Δ_{Kek} stand for the secular determinant appropriate to a single Kekulé structure, and E_{Kek} the corresponding energy. Then $E - E_{\text{Kek}}$ is merely the resonance energy R. So

$$R = E - E_{\text{Kek}} = \frac{\beta\gamma}{\pi i}\oint \frac{z}{\beta^2 - S^2z^2}\frac{d}{dz}\log\left(\frac{\Delta}{\Delta_{\text{Kek}}}\right)dz$$

Integration by parts, and the fact that, at large z, $\Delta/\Delta_{\text{Kek}} \longrightarrow 1$ allows this to be written (cf. Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1948, *A*, **195**, 188)

$$R = -\frac{\beta\gamma}{\pi i}\oint \frac{\beta^2 + S^2z^2}{(\beta^2 - S^2z^2)^2}\log\left(\frac{\Delta}{\Delta_{\text{Kek}}}\right)dz \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

This shows, as was noticed by de Heer, that the overlap integral exerts only a minor influence on the energies, since it appears only in the first factor under the integral, and occurs only as S^2 and higher powers. With $S \approx 0{\cdot}25$, these additional terms would be expected to be small.

The integration in (7) is straightforward, but must be done numerically. The contribution from the infinite semicircle vanishes so that it may be written

$$R = -\frac{\beta\gamma}{\pi}\int_{-\infty}^{\infty} \frac{\beta^2 - S^2y^2}{(\beta^2 + S^2y^2)^2}\log\left(\frac{\Delta(iy)}{\Delta_{\text{Kek}}(iy)}\right)dy \quad . \quad . \quad . \quad . \quad . \quad (8)$$

Numerical integration in the range $0 \leqslant |y/\beta| < 6$ and an estimate of the contribution from $|y/\beta| > 6$ in the same manner as used by Coulson and Jacobs (*J.*, 1949, 2805) usually provides a resonance energy of sufficient accuracy. But on account of the first factor in the integrand, the estimation of the contribution from $|y/\beta| > 6$ is not quite so simple as when $S = 0$. If there are n double bonds in the molecule, then $\Delta_{\text{Kek}}(z) = (z^2 - \beta^2)^n$. Also we may use the expansion of $\Delta(z)$ obtained by the author (*Proc. Camb. Phil. Soc.*, 1949, **43**, 202), *viz.*:

$$\Delta(z) = z^{2n} - C_2\beta^2z^{2n-2} + C_4\beta^4z^{2n-4} - \ldots \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

where C_2 = number of carbon–carbon bonds in the molecule, and C_4 = total number of pairs of non-contiguous bonds, etc. This means that

$$\log\left(\frac{\Delta(iy)}{\Delta_{\text{Kek}}(iy)}\right) = \frac{C_2 - n}{(y/\beta)^2} + \frac{2C_4 - C_2^2 + n}{2(y/\beta)^4} + \ldots \quad . \quad . \quad . \quad . \quad . \quad (10)$$

and the method of Coulson and Jacobs (*loc. cit.*) will apply.

It is possible, however, to reduce the contribution from $|y/\beta| > 6$ to negligible proportions as follows. In writing down Δ_{Kek}, let us suppose that the resonance integral is not β, but $x\beta$, where x is some constant to be chosen later. The corresponding overlap integral must be xS instead of S. No such modifications, however, are made in Δ. The form taken by (8) is now

$$R = \frac{\gamma}{\pi}\int_{-\infty}^{\infty} \frac{1 - S^2t^2}{(1 + S^2t^2)^2}\log\frac{\Delta(it)}{(t^2 + x^2)^n}dt \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

where we have introduced the dimensionless variable $t = y/\beta$. The expansion similar to (10) gives

$$\log\frac{\Delta(it)}{(t^2 + x^2)^n} = \frac{C_2 - nx^2}{t^2} + \frac{2C_4 - C_2^2 + nx^4}{2t^4} + \ldots \quad . \quad . \quad . \quad . \quad (12)$$

If we now choose x so that

$$C_2 - nx^2 = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

then (12) simplifies to

$$\log \frac{\Delta(it)}{(t^2 + x^2)^n} = \frac{2C_4 - C_2^2 + C_2^2/n}{2t^4} + \ldots \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

Explicit calculation for a variety of systems shows that the error resulting from complete neglect of that part of the integral in (11) which arises from $|t| > 6$ is less than $0{\cdot}01\gamma$. With this choice (13) for x, the energy of a Kekulé structure is

$$E_{\text{Kek}} = 2 \times \frac{nx\gamma}{1 + Sx} = \frac{2\sqrt{(nC_2)}}{1 + Sx}\gamma \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

Thus the total energy of the π-electrons in the original molecule is

$$E = \frac{2\sqrt{(nC_2)}\gamma}{1 + Sx} + \frac{2\gamma}{\pi}\int_0^\infty \frac{1 - S^2t^2}{(1 + S^2t^2)^2} \log \frac{\Delta(it)}{(t^2 + x^2)^n}\,\mathrm{d}t \quad . \quad . \quad . \quad (16)$$

where $x^2 = C_2/n$ and the effective range of integration is only $0 < t < 6$. Numerical integration presents no difficulties.

FIG. 1.

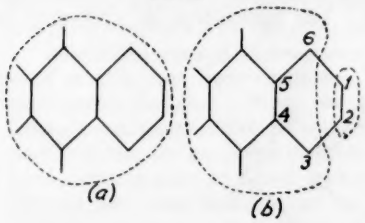
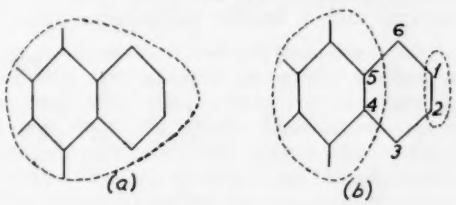


FIG. 2.



We have given this analysis in full. But our remaining applications of the method can be greatly abbreviated since they follow essentially the same basic idea.

Bond Localisation Energies.—The bond localisation energy (R. D. Brown, *Quart. Reviews*, 1952, **6**, 63) is defined as the energy necessary to localise a pair of π-electrons in a particular bond, which is supposed to be isolated from the rest of the resonating framework. Thus, in Fig. 1, the bond-localisation energy $E_{\text{bond loc.}}$ for the bond 1—2 is the difference in π-electron energies of the two systems shown as (*a*) and (*b*); in each case π-electrons are mobile within, but not across, the dotted lines. We are effectively comparing E for two systems. In the first system we take β as resonance integral for all the bonds: in the second we put $\beta_{16} = \beta_{23} = 0$, so that, in effect, no interaction can taken place across the bonds 1—6 and 2—3, leading to isolation of the two parts of the molecule. If Δ and Δ_b denote the secular determinants (without overlap) for these two systems, then by analogy with (8)

$$E_{\text{bond loc.}} = -\frac{\beta\gamma}{\pi}\int_{-\infty}^{\infty} \frac{\beta^2 - S^2y^2}{(\beta^2 + S^2y^2)^2} \log \frac{\Delta(iy)}{\Delta_b(iy)}\,\mathrm{d}y \quad . \quad . \quad . \quad . \quad (17)$$

There are the same number of carbon atoms in both structures, and so the expression Δ/Δ_b tends to unity quite fast as $y \longrightarrow \infty$. We may now expand (17) in the form (10) and use the method of Coulson and Jacobs for numerical integration. Alternatively we may improve the convergence by a process analogous to that used in passing from (8) to (16). If we introduce a fictitious β and S for the localised bond, with values $x\beta$, xS, but keep all the other non-vanishing β and S unchanged, then it may be shown, after a little reduction that

$$\log \frac{\Delta(iy)}{\Delta_b(iy)} = \frac{(3 - x^2)\beta^2}{y^2} + \ldots \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (18)$$

If we choose $x = \sqrt{3}$ we find that the contribution from values of $|y/\beta| > 6$ in (17) is quite negligible. Numerical integration is now straightforward. We can write

$$E_{\text{bond loc.}} = \left[\frac{2\sqrt{3}S}{1+\sqrt{3}S} - \frac{2S}{1+S}\right]\gamma - \frac{2\beta\gamma}{\pi}\int_0^\infty \frac{\beta^2 - S^2y^2}{(\beta^2 + S^2y^2)^2}\log\frac{\Delta(iy)}{\Delta_b^*(iy)}\,dy \quad . \quad (19)$$

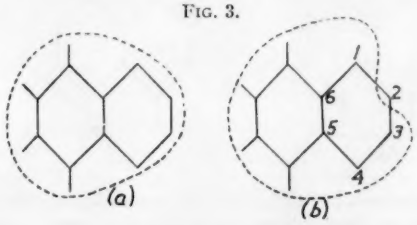
where Δ_b^* is the secular determinant for the fictitious system corresponding to Fig. 1*b* and in which β for the localised bond is replaced by $\beta\sqrt{3}$. The terms in square brackets in (19) are needed to correct for the false energy attributed to the isolated double bond 1—2 by the use of $x\beta$ instead of β. The relation between (19) and (16) is immediately clear if we recognise that a single Kekulé structure is one which we reach by successively localising double bonds in the manner of Fig. 1 until all the bonds are either single or double.

Para-localisation Energy.—The para-localisation energy is the energy required to localise two electrons on atoms which (Fig. 2) are *para* to each other. If we regard our previous bond-localisation as an ortho-process, then this is the corresponding para-process. Instead of (17) we shall have

$$E_{\text{para. loc.}} = -\frac{\beta\gamma}{\pi}\int_{-\infty}^{\infty}\frac{\beta^2 - S^2y^2}{(\beta^2 + S^2y^2)^2}\log\frac{\Delta(iy)}{\Delta_p(iy)}\,dy \quad . \quad . \quad . \quad . \quad (20)$$

where Δ_p is the secular determinant for the system, such as in Fig. 2*b*, consisting of two isolated atoms (here 3 and 6) with one π-electron each, and the residual molecule (here ethylene and a smaller polynuclear hydrocarbon). The integration in (20) may be

FIG. 3.



performed without difficulty; but it is a little more tedious since $\Delta_p(z)$ contains a factor z^2 arising from the isolated atoms (here 3 and 6). This factor causes a logarithmic infinity in the integrand near $z = 0$. We cannot merely leave this factor out because the convergence of (20) at large y then becomes too slow for convenience. But if, for mathematical convenience, we imagine the *para*-atoms to be joined by a fictitious bond with resonance integral $x\beta$, we avoid the logarithmic infinity at the origin, and we reduce the integrand to very small values at large y by putting $x = 2$. The new formula which replaces (20) is

$$E_{\text{para. loc.}} = \frac{4S\gamma}{1+2S} - \frac{2\beta\gamma}{\pi}\int_0^\infty \frac{\beta^2 - S^2y^2}{(\beta^2 + S^2y^2)^2}\log\frac{\Delta(iy)}{\Delta_p^*(iy)}\,dy \quad . \quad . \quad . \quad (21)$$

where

$$\Delta_p^*(iy) = \Delta_p(iy) \times (y^2 + 4\beta^2)/y^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (22)$$

The first term on the right in (21) is needed to compensate for the fictitious bond which we have introduced between atoms 6 and 3. Despite its appearance $\Delta_p^*(iy)$ is finite at $y = 0$. In this way para-localisation energies are found by one single integration.

Atom-localisation Energy.—The atom localisation energy, $E_{\text{atom loc.}}$, was originally introduced by Wheland (*J. Amer. Chem. Soc.*, 1942, **64**, 900) in a discussion of the transition state in chemical reactions. According as the reaction is electrophilic, free-radical, or nucleophilic, we require to localise 2, 1, or 0 electrons on one particular atom (*e.g.*, atom 2 in Fig. 3). This means that we have $2n - 2$, $2n - 1$, or $2n$ electrons in the residual molecule shown within the broken lines in Fig. 3*b*. This is an odd alternant, so that the top occupied orbital has zero energy. As a result—a situation already recognised by

several writers—the localisation energy, $E_{\text{atom loc.}}$, is the same for all three types of reaction. An analysis very similar to that which led up to (20) shows that we may write

$$E_{\text{atom loc.}} = -\frac{\beta\gamma}{\pi}\int_{-\infty}^{\infty}\frac{\beta^2 - S^2y^2}{(\beta^2 + S^2y^2)^2}\log\frac{\Delta(iy)}{\Delta_a(iy)}\,dy \quad . \quad . \quad . \quad . \quad (23)$$

where Δ_a is the secular determinant Δ with (in the particular case of Fig. 3) $\beta_{21} = 0 = \beta_{23}$. Once again Δ_a involves a factor y^2 so that the numerical integration has to deal with a logarithmic infinity at $y = 0$. Just as in (21) this may be much simplified, both at $y = 0$ and $y = \infty$, by a transformation to

$$E_{\text{atom loc.}} = \frac{2\sqrt{2S}\gamma}{1 + \sqrt{2S}} - \frac{2\beta\gamma}{\pi}\int_{0}^{\infty}\frac{(\beta^2 - S^2y^2)}{(\beta^2 + S^2y^2)^2}\log\frac{\Delta(iy)}{\Delta_a{}^*(iy)}\,dy \quad . \quad . \quad (24)$$

where

$$\Delta_a{}^*(iy) = \Delta_a(iy) \times (y^2 + 2\beta^2)/y^2 \quad . \quad . \quad . \quad . \quad . \quad (25)$$

The advantage of equations (16), (19), (21), and (24) is that they reduce the calculation of the various resonance and localisation energies to the evaluation of one single integral. On account of the fact that in each case the integrand tends to zero very rapidly as y increases, the contribution from $|y/\beta| > 6$ is negligible for almost all purposes. Furthermore these energies are given directly, and are not obtained as the relatively small differences between two fairly large and nearly equal energies. This greatly increases the accuracy available with the same amount of numerical effort.

Non-alternants and Heteromolecules.—Our previous discussion has dealt solely with the case of alternant hydrocarbons. These are the systems most commonly studied, and most easily handled. When we are concerned with non-alternant hydrocarbons (*e.g.*, fulvene, azulene) or heterocyclic systems (*e.g.*, pyridine) general formulations like our previous ones are no longer possible. But in any particular case formulæ which serve the same purpose may be found without difficulty. We can no longer use the relationships (1)—(3), but must deal all the time with the full secular determinant (Δ_0 say) involving S and the various α's. Instead of using (5) and (6) as our starting point, we must fall back on the more cumbrous formula

$$E = \frac{1}{\pi i}\oint\frac{z\Delta_0{}'(z)}{\Delta_0(z)}\,dz \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (26)$$

This leads to the resonance energy formula

$$R = \frac{1}{\pi i}\oint z\frac{d}{dz}\log\left(\frac{\Delta_0(z)}{\Delta_{0,\,\text{Kek}}(z)}\right)dz \quad . \quad . \quad . \quad . \quad . \quad . \quad (27)$$

where $\Delta_{0,\,\text{Kek}}$ is the secular determinant, including S and α, for a Kekulé structure. This may be converted into

$$R = -\frac{1}{\pi i}\oint\log\left(\frac{\Delta_0(z)}{\Delta_{0,\,\text{Kek}}(z)}\right)dz \quad . \quad . \quad . \quad . \quad . \quad . \quad (28)$$

and so into an integral along the y-axis. But, on account of the complex character of $\Delta_0(iy)$, the whole analysis becomes more clumsy. For that reason we shall not here attempt to go beyond (28).

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The Chemistry of Fluorene. Part IV. Some New Chloro- and Nitro-derivatives.*

By E. J. Greenhow, A. S. Harris, and E. N. White.

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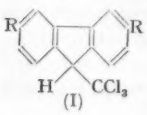
Attempts to synthesise 9-trichloromethylfluorene and 9-(1 : 1-dichloroethyl)fluorene were unsuccessful owing, it is believed, to the ease with which they lose hydrogen chloride to yield 9-dichloromethylenefluorene and 9-1′-chloroethylidenefluorene (or 9-1′-chlorovinylfluorene) respectively. 9-Dichloromethylfluorene and 9 : 10-dichlorophenanthrene were obtained from 9-formylfluorene and phosphorus pentachloride; the former product was readily dehydrochlorinated to 9-chloromethylenefluorene. With thionyl chloride 9-formylfluorene yielded 9 : 9′-diformyl-9 : 9′-difluorenyl and 9-acetylfluorene yielded 9-acetyl-9-chlorofluorene which was readily converted into 9 : 9′-diacetyl-9 : 9′-difluorenyl.

9 : 9-Dichlorofluorene was prepared from fluorene and carbon tetrachloride in the presence of benzyltrimethylammonium hydroxide, while 2 : 5 : 9 : 9-tetrachloro- and 5-nitro-2 : 9 : 9-trichloro-fluorene were obtained from 2 : 5-dinitrofluorenone and phosphorus pentachloride. Direct addition of chlorine to fluorene yielded a hexachloride and a complex mixture of polychlorofluorenes. Of these compounds, only 9 : 9-dichlorofluorene is active as an insecticide.

Although fluorene-9-carboxylic acid shows activity as a plant-growth promoter the 2 : 7-dichloro-derivative does not.

Although it is known that 1 : 3 : 6 : 8-tetranitro- and 1 : 8-dichloro-3 : 6-dinitro-carbazole



(I)

are fungicidal (B.I.O.S. Final Report, No. 1480; F.I.A.T. Final Report, No. 949) and 1 : 1 : 1-trichloro-2 : 2-di-*p*-chlorophenylethane (D.D.T.) and "benzene hexachloride" (γ-isomer) are established insecticides, there is no record of the efficacy of the analogous fluorene derivatives. Indeed the fluorene analogues of D.D.T. (I; R = Cl) and benzene hexachloride are unknown and only a few polychloro-, polynitro- and chloronitro-fluorenes have been reported.

In attempts to synthesise 9-trichloromethylfluorene (I; R = H), chlorination of 9-methylfluorene in ultra-violet light gave, as the only substance isolated, poly-(9-methylenefluorene), presumably formed by way of 9-chloro-9-methylfluorene (cf. Wieland and Krause, *Annalen*, 1925, **443**, 135). In the absence of ultra-violet light, nuclear chlorination occurred to yield 2 : 7-dichloro-9-methylfluorene, the identity of which was established by oxidation to 2 : 7-dichlorofluorenone. No reaction occurred when 4 : 4′-dichlorodiphenyl was treated with chloral hydrate in the presence of sulphuric acid; with warm chlorosulphonic acid 2 : 7-dichlorodibenzothiophen dioxide was formed in a manner analogous to that used by Courtot and Lin (*Bull. Soc. chim.*, 1931, **49**, 1047) for the preparation of the corresponding dibromo-compound.

9-Dichloromethylenefluorene did not add hydrogen chloride in any conditions tried. The exocyclic double bond was very inert since bromination and chlorination yielded the corresponding 2 : 7-disubstituted derivatives and nitration gave 9-dichloromethylene-2-nitro-fluorene.

Condensation of fluorene and 9-fluorenylsodium with carbon tetrachloride were also tried as a possible route to 9-trichloromethylfluorene. There was no reaction when fluorene, carbon tetrachloride, ethanol, and sodium ethoxide were refluxed but, after fluorene and benzyltrimethylammonium hydroxide in carbon tetrachloride had been exposed to daylight for three months, 9 : 9-dichlorofluorene and fluorenone were isolated. It is believed that the dichlorofluorene is formed by a free-radical photochemical reaction in the first stage of which carbon tetrachloride decomposes into chlorine radicals and trichloromethyl radicals. Bowen and Rohatgi (*Discuss. Faraday Soc.*, 1953, **14**, 146) obtained 9-chloro- and

* Part III, *J.*, 1953, 3099.

9 : 10-dichloro-anthracene on irradiation of anthracene in carbon tetrachloride with ultra-violet light, presumably by a similar mechanism. Condensation of carbon tetrachloride and 9-fluorenylsodium yielded 9-dichloromethylenefluorene in addition to fluorene and di-9-fluorenyl, which suggests that the trichloromethyl compound, if first formed, readily loses a molecule of hydrogen chloride. This view is consistent with the known stability of the dibenzofulvene structure and is supported by the fact that 9-dichloromethylfluorene and crude 9-(1 : 1-dichloroethyl)fluorene which were prepared by reaction of phosphorus pentachloride with 9-formyl- and 9-acetyl-fluorene were converted into 9-chloromethylene-fluorene and 9-1′-chloroethylidenefluorene, respectively, when passed through activated alumina.

A minor product from the reaction of 9-formylfluorene and phosphorus pentachloride is 9 : 10-dichlorophenanthrene which must be formed either by a rearrangement during dehydrochlorination of 9-chloro-9-dichloromethylfluorene (cf. Wittig, Davis, and Koenig, *Ber.*, 1951, **84**, 627) or by chlorination of 9-chlorophenanthrene produced by a similar rearrangement during dehydrochlorination of 9-dichloromethylfluorene.

Distillation *in vacuo* of the product from 9-acetylfluorene and phosphorus pentachloride resulted in vigorous decomposition and gave 9-1′-chlorovinylfluorene in very low yield. This compound and 9-1′-chloroethylidenefluorene were identified by their infra-red and ultra-violet absorption spectra and by catalytic hydrogenation to 9-1′-chloroethylfluorene which was also prepared by the reaction of 9-1′-hydroxyethylfluorene with thionyl chloride.

It was expected that thionyl chloride would react with the enolic form of 9-acetylfluorene to yield 9-1′-chloroethylidenefluorene but the main product proved to be 9-acetyl-9-chloro-fluorene which was readily converted by copper powder into 9 : 9′-diacetyl-9 ; 9′-difluorenyl. The diacetyl compound ($C_{30}H_{24}O_2$) was identical with the alleged dimer of 9-acetylfluorene ($C_{30}H_{22}O_2$) described by Von and Wagner (*J. Org. Chem.*, 1944, **9**, 155). Both 9-acetyl-9-chlorofluorene and 9 : 9′-diacetyl-9 : 9′-difluorenyl were converted into 9 : 9′-difluorenyl by boiling alcoholic potassium hydroxide. With 9-formylfluorene thionyl chloride gave only 9 : 9′-diformyl-9 : 9′-difluorenyl.

When fluorene in carbon tetrachloride was treated with dry chlorine at 15° in sunlight or ultra-violet light, a clear viscous oil was obtained from which a crystalline hexachloride was isolated. This substance was readily oxidised to a hexachlorohexahydrofluorenone and its ultra-violet absorption spectrum showed it to have a non-aromatic structure; it forms a trichlorofluorene on dehydrohalogenation. The ether-soluble portion of the product was high-boiling and inseparable, probably composed of polychlorofluorenes.

2 : 5 : 9 : 9-Tetrachlorofluorene was prepared from 2 : 5-dinitrofluorenone and phosphorus pentachloride at 170—180° (see Schmidt and Wagner, *Annalen*, 1912, **387**, 159, for the similar synthesis of 2 : 7 : 9 : 9-tetrachlorofluorene). At a lower temperature both 9 : 9-dichloro-2 : 5-dinitrofluorene and a trichloromononitrofluorene were obtained. Since it is known that the 2-nitro-group of 2 : 5-dinitrofluorenone is more reactive than that in the 5-position, *e.g.*, partial reduction yields 2-amino-5-nitrofluorenone (Courtot and Moreaux, *Compt. rend.*, 1943, **217**, 453), the mononitro-compound is assumed to be 2 : 9 : 9-trichloro-5-nitrofluorene. Acid hydrolysis of the substituted 9 : 9-dichlorofluorenes gave the corresponding fluorenones.

Wain (Roy. Inst. Chem. Monograph, 1953, No. 2, p. 7) has reported that whereas fluorene-9-carboxylic acid is a plant-growth hormone, its 9-methyl derivative is inactive and he suggests that activity is associated with the presence of a $C_{(9)}$-hydrogen atom. As certain ring-chlorinated phenoxyacetic acids are highly active plant-growth hormones although the parent phenoxyacetic acid is inactive (Wain, *ibid*, p. 5), 2 : 7-dichloro-fluorene-9-carboxylic acid was prepared for evaluation. It was obtained by chlorination of fluorene-9-carboxylic acid in chloroform, but could not be prepared by carboxylation of 9-(2 : 7-dichlorofluorenyl)sodium since 2 : 7-dichlorofluorene did not react with sodamide in decalin. This failure to form a sodio-derivative and the inactivity of 2 : 7-dichloro-fluorene-9-carboxylic acid as a plant-growth promoter are no doubt due to deactivation of the 9-hydrogen atoms by the chlorine in the 2- and the 7-position.

Of the chloro- and nitro-fluorenes described above, only 9 : 9-dichlorofluorene was active against *Calliphora*. 2 : 7 : 9 : 9-Tetrachloro- and 9 : 9-dichloro-fluorene were non-

toxic to the grain weevil (*Calandra granara*) and locust (*Locusta migratoria*), and the latter compound was also inactive against the mosquito (*Aedis aegypti*) and housefly (*Musca domestica*).

Experimental

2 : 7-*Dichloro*-9-*methylfluorene*.—A slow stream of chlorine was passed for 2 hr. through a solution of 9-methylfluorene (5 g.) in carbon tetrachloride (50 c.c.) at room temperature. Evaporation *in vacuo* gave a viscous oil from which 2 : 7-*dichloro*-9-*methylfluorene* slowly crystallised. After it had been freed from oil by washing with cold light petroleum (b. p. 40—60°), the compound crystallised from ethanol as white plates, m. p. 132—133° (Found: C, 67·2; H, 4·0; Cl, 28·2. $C_{14}H_{10}Cl_2$ requires C, 67·5; H, 4·0; Cl, 28·5%). Oxidation with chromic oxide in acetic acid gave 2 : 7-dichlorofluorenone, m. p. and mixed m. p. with a specimen prepared from 2 : 7-dichlorofluorene, 190°.

Experiments with 9-*Dichloromethylenefluorene*.—(*a*) 9-Dichloromethylenefluorene (Staudinger, *Helv. Chim. Acta*, 1920, **3**, 840) (0·5 g.) in carbon tetrachloride (5 c.c.) was treated with bromine (0·5 g.) and iodine (0·1 g.) in carbon tetrachloride (20 c.c.). Rapid bromination occurred on gentle warming and 2 : 7-*dibromo*-9-*dichloromethylenefluorene* gradually crystallised. After being filtered off, washed with carbon tetrachloride, and crystallised from acetic acid, the compound formed yellow needles (0·5 g.), m. p. 237—238° (Found: C, 41·7; H, 1·6. $C_{14}H_6Cl_2Br_2$ requires C, 41·5; H, 1·5%). In the absence of iodine only unchanged 9-dichloromethylenefluorene was obtained.

(*b*) Chlorine was passed through 9-dichloromethylenefluorene (2 g.) in chloroform (50 c.c.) at 18—22° for 10 hr. 2 : 7-*Dichloro*-9-*dichloromethylenefluorene* was deposited as a yellow solid which crystallised from toluene as needles (0·8 g.), m. p. 242—244° (Found: C, 52·7; H, 2·05; Cl, 44·4. $C_{14}H_6Cl_4$ requires C, 53·1; H, 1·9; Cl, 44·9%). The ultra-violet absorption spectrum, like that of the corresponding dibromo-compound, is of the 9-ethylidenefluorene type (see Table). Oxidation with chromic oxide in acetic acid gave 2 : 7-dichlorofluorenone, m. p. and mixed m. p. 189—190°).

(*c*) 9-Dichloromethylenefluorene (2 g.) was added portionwise to nitric acid (7·5 c.c.; *d* 1·42) and acetic acid (15 c.c.). After it had been stirred for 1 hr., the mixture was stored for 24 hr. and the yellow solid was then filtered off (2·3 g.). Chromatography on alumina gave 9-*dichloromethylene*-2-*nitrofluorene* (0·8 g.), yellow needles (from acetic acid), m. p. 199—200° (Found: C, 57·1; H, 2·5; Cl, 24·6; N, 4·6. $C_{14}H_7O_2NCl_2$ requires C, 57·5; H, 2·4; Cl, 24·3; N, 4·8%). Oxidation with chromic acid gave 2-nitrofluorenone, m. p. and mixed m. p. 222—223°.

Attempt to Condense 4 : 4′-*Dichlorodiphenyl and Chloral Hydrate*.—Chlorosulphonic acid (3·5 c.c.) was slowly added to 4 : 4′-dichlorodiphenyl (5·6 g.) and chloral hydrate (4·1 g.), and the mixture was stirred for 5 hr. at 80°, then diluted with water. The insoluble material was filtered off and crystallised from acetic acid to give 2 : 7-dichlorodibenzothiophen 9 : 9-dioxide (2·2 g.), m. p. 295—296° (Found: C, 50·6; H, 2·2. Calc. for $C_{12}H_6O_2SCl_2$: C, 50·5; H, 2·1%).

Reaction of Fluorene and Carbon Tetrachloride.—Fluorene (10 g.), benzyltrimethylammonium hydroxide (10 c.c. of a 40% solution in *n*-butanol), and carbon tetrachloride (100 c.c.) were stored for 3 months at room temperature in daylight. After it had been washed with dilute hydrochloric acid and water, the solution was dried and evaporated, to give an orange solid (9·2 g.). Crystallisation from ethanol gave fluorene (4·5 g.) and 9 : 9-dichlorofluorene (3·2 g.), m. p. and mixed m. p. 98—100°. The filtrate, after evaporation, was chromatographed on alumina to give fluorenone (1·1 g.).

Condensation of 9-*Fluorenylsodium and Carbon Tetrachloride*.—9-Fluorenylsodium (70 g.), carbon tetrachloride (100 c.c.), and light petroleum (b. p. 60—80°; 300 c.c.) were refluxed for 60 hr. The product was filtered to remove sodium chloride (23 g.), and the filtrate evaporated to leave a dark oil (56 g.). The latter when chromatographed on alumina (30 × 1¼ in.) yielded successively fluorene (21 g.), 9-dichloromethylenefluorene (4·3 g.), 9 : 9′-difluorenyl (5·4 g.), and an amorphous brown powder (22 g.) which could not be purified further. The dichloro-compound crystallised from methanol as needles, m. p. and mixed m. p. 127—128°, and formed a picrate (in acetic acid), m. p. 172—173°. The ultra-violet spectrum (Table) is similar to that of 9-ethylidenefluorene.

Reaction of 9-*Formylfluorene and Phosphorus Pentachloride*.—Freshly prepared 9-formylfluorene (10 g.) and phosphorus pentachloride (11 g.) were heated at 150° for 2 hr. Phosphorus oxychloride was distilled off continuously and its removal completed at reduced pressure. The residue distilled as a yellow viscous oil (5 g.), b. p. 175—180°/5 mm., which slowly solidified.

Several crystallisations from light petroleum (b. p. 60—80°) gave 9-*dichloromethylfluorene* as white plates, m. p. 106° (Found : C, 67·5; H, 4·2; Cl, 28·0. $C_{14}H_{10}Cl_2$ requires C, 67·5; H, 4·0; Cl, 28·5%). The compound did not form a picrate and when refluxed with alcoholic potassium hydroxide was converted into fluorene. When 9-dichloromethylfluorene in light petroleum (b. p. 60—80°) was adsorbed on activated alumina it was quantitatively dehydrochlorinated to 9-*chloromethylenefluorene* which crystallised from ethanol or light petroleum as white needles, m. p. 74—75° (Found : C, 78·9; H, 4·2; Cl, 17·0. $C_{14}H_9Cl$ requires C, 79·1; H, 4·2; Cl, 16·7%). The infra-red spectrum shows a band due to a trisubstituted ethylene and the ultra-violet spectrum is of the 9-ethylidenefluorene type (see Table). The *picrate*, orange needles (from benzene), had m. p. 141—142° (Found : C, 54·1; H, 2·8; N, 9·4. $C_{20}H_{12}O_7N_3Cl$ requires C, 54·4; H, 2·7; N, 9·5%). Concentration of the light petroleum filtrate from the first crystallisation of 9-dichloromethylfluorene led to the isolation of 9 : 10-dichlorophenanthrene (0·2 g.), white needles, m. p. and mixed m. p. 165° (Found : C, 68·1; H, 3·2; Cl, 28·5. Calc. for $C_{14}H_8Cl_2$: C, 68·0; H, 3·3; Cl, 28·7%).

Reaction of 9-Acetylfluorene and Phosphorus Pentachloride.—Freshly prepared 9-acetylfluorene (10 g.) and phosphorus pentachloride (10 g.) were heated at 150° for 1½ hr. and phosphorus oxychloride was continuously distilled from the mixture. The residue started to distil at 170—180°/5 mm., but when only a small amount of distillate had been collected a vigorous decomposition occurred and the mixture after foaming considerably formed a soft coke. The distillate (2 g.), which solidified on cooling, was crystallised from light petroleum (b. p. 60—80°), to give 9-1′-*chlorovinylfluorene* as white needles, m. p. 81—82° (Found : C, 79·6; H, 5·0; Cl, 15·4. $C_{15}H_{11}Cl$ requires C, 79·5; H, 4·9; Cl, 15·6%). The compound did not form a picrate and was not changed by chromatography on activated alumina. Infra-red examination showed the presence of the $CH_2{:}C<$ group; the ultra-violet spectrum is similar to that of fluorene (Table).

In a further experiment the products from the reaction of 9-acetylfluorene and phosphorus pentachloride were passed in benzene through a small alumina column to remove coloured impurities. Evaporation of the eluate gave a pale brown oil which was partly soluble in light petroleum (b. p. 60—80°). The soluble portion was adsorbed on an alumina column (20 × 1 in.). A mixture of benzene and light petroleum eluted 9-1′-*chloroethylidenefluorene* (2·5 g.) which crystallised from light petroleum as white needles, m. p. 91·5—92·5° (Found : C, 79·6; H, 4·9; Cl, 15·5. $C_{15}H_{11}Cl$ requires C, 79·5; H, 4·9; Cl, 15·6%). A methyl group and a fully substituted ethylene structure were shown to be present by infra-red examination. The compound formed a *picrate*, orange needles (from benzene), m. p. 181—182° (Found : C, 55·2; H, 3·3; N, 9·0. $C_{21}H_{14}O_7N_3Cl$ requires C, 55·3; H, 3·1; N, 9·2%). No 9-1′-chlorovinylfluorene was isolated from the chromatographic fractions.

9-1′-*Chloroethylfluorene.*—(*a*) 9-1′-Hydroxyethylfluorene (1 g.) and thionyl chloride (10 c.c.) were heated under reflux for 1 hr. Unchanged thionyl chloride was distilled off, the residue was dissolved in ether, and the solution washed with water, dried, and evaporated. The residual oil was freed from traces of unchanged hydroxyethylfluorene by chromatography on activated alumina, light petroleum eluting the less strongly adsorbed *chloroethyl* compound which was obtained as a colourless oil, n_D^{25} 1·630 (Found : C, 78·9; H, 5·5; Cl, 15·4. $C_{15}H_{13}Cl$ requires C, 78·8; H, 5·7; Cl, 15·5%).

(*b*) 9-1′-Chlorovinylfluorene (0·5 g.) in acetic acid (20 c.c.) was shaken with hydrogen in the presence of pre-reduced Adams's catalyst (0·1 g.). When 1 mol. of hydrogen had been absorbed, the mixture was filtered and crude 9-1′-chloroethylfluorene was obtained by evaporation of the filtrate. Impurities were removed by chromatography on activated alumina to give a colourless oil (0·4 g.), the infra-red absorption spectrum of which was identical with that of the compound prepared by method (*a*).

(*c*) 9-1′-Chloroethylidenefluorene was hydrogenated in the same way as the chlorovinyl compound. Infra-red spectroscopy showed that the product was again 9-1′-chloroethylfluorene.

9-*Acetyl*-9-*chlorofluorene.*—9-Acetylfluorene (5 g.) and thionyl chloride (20 c.c.) were heated under reflux for 4 hr. Excess of thionyl chloride was distilled off under reduced pressure and the residue extracted with light petroleum (b. p. 60—80°). The extract was washed with water, dried, and evaporated to give an oil which slowly solidified. Crystallisation from ethanol (charcoal) gave 9-*acetyl*-9-*chlorofluorene* as white needles (1·5 g.), m. p. 100° (Found : C, 74·1; H, 4·8; Cl, 14·5. $C_{15}H_{11}OCl$ requires C, 74·2; H, 4·6; Cl, 14·6%). When the compound was heated under reflux with alcoholic potassium hydroxide it was converted into 9 : 9′-difluorenyl, m. p. 245—246°.

9 : 9′-*Diacetyl*-9 : 9′-*difluorenyl.*—9-Chloro-9-acetylfluorene (0·25 g.) and copper powder

(0·4 g.) were heated in boiling benzene (30 c.c.) for 6 hr. The solution was filtered and the filtrate evaporated, to give the *diacetyl*-compound (quantitative yield), white prisms (from benzene–light petroleum), m. p. 241—242° (Found: C, 87·2; H, 5·4; $C_{30}H_{24}O_2$ requires C, 86·9; H, 5·35%). This was converted by boiling alcoholic potassium hydroxide into 9 : 9′-difluorenyl, m. p. 245—246°.

9 : 9′-*Diformyl*-9 : 9′-*difluorenyl*.—9-Formylfluorene (3 g.), thionyl chloride (5 c.c.), and dry ether (20 c.c.) were heated under reflux for 1 hr. On cooling, the diformyl derivative separated as a white solid (1·6 g.) which crystallised from benzene as prisms, m. p. 217—218° (Found: C, 86·7; H, 4·7. Calc. for $C_{28}H_{18}O_2$: C, 87·0; H, 4·7%), converted by boiling alcoholic potassium hydroxide into 9 : 9′-difluorenyl, m. p. 245—246°.

Chlorination of Fluorene.—Dry chlorine was passed into fluorene (50 g.) in carbon tetrachloride (800 c.c.) at 15° for 9 hr. in bright sunlight. After it had been freed from chlorine by bubbling of air through it, the solution was evaporated *in vacuo* on the water-bath, to leave a clear viscous oil (101 g.) which was dissolved in ether and stored at 0°. The white precipitate (20·5 g.) was filtered off and crystallised from acetic acid, to give *fluorene hexachloride*, prisms, m. p. 215—217° (Found: C, 41·4; H, 2·65; Cl, 56·5. $C_{13}H_{10}Cl_6$ requires C, 41·1; H, 2·6; Cl, 56·2%).

The hexachloride (0·5 g.) was oxidised with chromic oxide (1·0 g.) in boiling acetic acid (10 c.c.) to a *hexachlorohexahydrofluorenone* (0·2 g.), prisms (from acetic acid), m. p. 193—194° (Found: C, 39·6; H, 2·1; Cl, 53·8. $C_{13}H_6OCl_6$ requires C, 39·7; H, 2·0; Cl, 54·2%). The infra-red spectrum showed the presence of a carbonyl group.

The fluorene hexachloride (1 g.) was treated for 3 hr. with potassium hydroxide (5 g.) in boiling ethanol (50 c.c.). The brown solid product, chromatographed on alumina, gave a *trichlorofluorene* (0·1 g.), white needles (from ethanol), m. p. 102—103° (Found: C, 57·3; H, 2·4; Cl, 39·0. $C_{13}H_7Cl_3$ requires C, 57·8; H, 2·6; Cl, 39·6%). The ultra-violet spectrum resembles that of fluorene (Table).

Reaction of 2 : 5-*Dinitrofluorenone and Phosphorus Pentachloride*.—(*a*) 2 : 5-Dinitrofluorenone (5 g.) and phosphorus pentachloride (12·5 g.) were heated at 170—180° for 6 hr. in a sealed tube. The cooled product was treated with ice and water, and the insoluble material filtered off, washed, and dried. Crystallisation from ethanol gave 2 : 5 : 9 : 9-*tetrachlorofluorene* (3·2 g.), white needles, m. p. 148—149° (Found: C, 50·8; H, 2·05; Cl, 47·2. $C_{13}H_6Cl_4$ requires C, 51·3; H, 2·0; Cl, 46·7%).

2 : 5 : 9 : 9-Tetrachlorofluorene (0·4 g.), acetic acid (5 c.c.), concentrated hydrochloric acid (1 c.c.), and water (15 c.c.) were heated under reflux for 4 hr. The product was extracted with ether, and the extract washed with sodium hydrogen carbonate solution and water, dried ($MgSO_4$), and evaporated to yield 2 : 5-*dichlorofluorenone* (0·24 g.); recrystallisation from *n*-propanol gave yellow needles, m. p. 151—152° (Found: C, 62·3; H, 2·3; Cl, 29·2. $C_{13}H_6OCl_2$ requires C, 62·65; H, 2·4; Cl, 28·6%). The *phenylhydrazone* crystallised from ethanol as needles, m. p. 162—163° (Found: C, 66·8; H, 3·4; Cl, 21·2; N, 7·9. $C_{19}H_{12}N_2Cl_2$ requires C, 67·3; H, 3·5; Cl, 20·9; N, 8·3%).

(*b*) 2 : 5-Dinitrofluorenone (9·5 g.) and phosphorus pentachloride (15 g.) were heated at 140° for 20 hr. in a sealed tube. The product was cooled and poured into ice and water, and the insoluble brown solid (10 g.) was filtered off, washed with water, and dried at 100°. Chromatography on alumina (30 × 1¼ in.) gave 2 : 9 : 9-*trichloro*-5-*nitrofluorene* (3·6 g.), yellow needles (from *n*-propanol), m. p. 170—171° (Found: C, 49·9; H, 2·0; Cl, 33·3. $C_{13}H_6O_2NCl_3$ requires C, 49·6; H, 1·9; Cl, 33·8%), followed by 9 : 9-*dichloro*-2 : 5-*dinitrofluorene* (3·2 g.), yellow prisms (from acetic acid), m. p. 212—213° (Found: C, 48·5; H, 1·9; Cl, 21·2; N, 8·3. $C_{13}H_6O_4N_2Cl_2$ requires C, 48·0; H, 1·85; Cl, 21·8; N, 8·6%).

2 : 9 : 9-Trichloro-5-nitrofluorene (0·6 g.), acetic acid (7·5 c.c.), concentrated hydrochloric acid (1·5 c.c.), and water (22·5 c.c.) were heated under reflux for 4 hr. 2-*Chloro*-5-*nitrofluorenone* was filtered off, washed with water, and dried at 100°. It crystallised from *n*-propanol as yellow needles (0·4 g.), m. p. 174—175° (Found: C, 59·7; H, 2·4; Cl, 13·5; N, 5·2. $C_{13}H_6O_3NCl$ requires C, 60·2; H, 2·3; Cl, 13·7; N, 5·4%).

9 : 9-Dichloro-2 : 5-dinitrofluorene (1 g.), when hydrolysed similarly, gave 2 : 5-dinitrofluorenone (0·7 g.), yellow needles (from acetic acid), m. p. and mixed m. p. 241—243° (Found: C, 58·2; H, 2·3; N, 10·1. Calc. for $C_{13}H_6O_5N_2$: C, 57·8; H, 2·2; N, 10·4%).

2 : 7-*Dichlorofluorene*-9-*carboxylic Acid*.—Dry chlorine was passed into fluorene-9-carboxylic acid (6 g.) in chloroform (150 c.c.) at 20° for 6 hr. The solution was evaporated under nitrogen, and the oily residue diluted with light petroleum (b. p. 40—60°; 100 c.c.) to give 2 : 7-*dichlorofluorene*-9-*carboxylic acid* (3·3 g.). Crystallisation from acetic acid yielded white prisms, m. p. 253—254° (decomp.) (Found: C, 60·1; H, 3·0; Cl, 24·8. $C_{14}H_8O_2Cl_2$ requires C, 60·2; H, 2·9;

Cl, 25·4%). Oxidation with sodium dichromate in acetic acid gave 2 : 7-dichlorofluorenone, m. p. and mixed m. p. 190—190·5°. The ultra-violet spectrum of the acid was similar to that of fluorene (Table).

Absorption spectra (*maxima, in* Å, *followed by log* ε).

9-Ethylidenefluorene	2300	2465	2555	2710	2800	2970	3110
	4·61	4·46	4·60	4·13	4·15	4·03	4·00
9-1′-Chloroethylidenefluorene	2300	2500	2575	2700	2800	3025	3150
	4·47	4·49	4·59	4·20	4·20	4·09	4·11
9-Chloromethylenefluorene	2300	2475	2575	2700	2800	3000	3125
	4·45	4·52	4·66	4·13	4·13	4·04	4·00
9-Dichloromethylenefluorene	2275	2500	2600	2700	2800	3050	3175
	4·37	4·50	4·66	4·19	4·20	4·12	4·17
2 : 7-Dichloro-9-dichloromethylenefluorene	2300	2575	2650	2750	2850	3050	3200
	4·43	4·57	4·69	4·34	4·37	4·25	4·21
2 : 7-Dibromo-9-dichloromethylenefluorene	2300	2575	2675	2750 *	2875	3075	3200
	4·43	4·58	4·75	4·36	4·36	4·29	4·20
Fluorene	2260 *	2545 *	2610	2710 *	2885	3000	
	3·86	4·20	4·24	4·10	3·78	3·94	
Trichlorofluorene	2300	2625	2700	2825 *	2950	3075	
	4·40	4·20	4·27	4·07	3·89	3·45	
9-1′-Chlorovinylfluorene	2280 *	2580 *	2650	2750	2900	3025	
	3·97	4·18	4·25	4·10	3·61	3·68	
2 : 7-Dichlorofluorene-9-carboxylic acid	—	2650 *	2750	2825 *	3000	3100	
	—	4·28	4·35	4·24	3·87	3·89	

* Inflection.

Absorption Spectra.—Ultra-violet absorption spectra (shown above) were determined in absolute ethanol with a Hilger " Uvispek " spectrophotometer. Infra-red absorption spectra were measured with a Grubb Parsons S3A single-beam spectrometer, the powdered specimens being suspended in " Nujol."

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Oxidations with Phenyl Iodosoacetate. Part III. Primary Aromatic Amines in Acetic Acid.*

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The oxidation of a primary aromatic amine with phenyl iodosoacetate in acetic acid solution yields generally the corresponding azo-compound. *o*-Nitroamines do not yield the furazan oxides which are formed in high yields in benzene solution (Part II).

In Part II * it was shown that a number of primary aromatic amines were oxidised by phenyl iodosoacetate in benzene solution to the corresponding azo-compounds in yields ranging from traces to almost quantitative, 1—2 mol. of reagent being consumed. Certain amines yielded other products: *o*-nitroanilines, for instance, formed the corresponding furazan oxides in high yield.

The action of phenyl iodosoacetate in acetic acid solution on a number of primary aromatic amines has now been examined. Except as noted in the Table, the uptakes had reached the values shown in 24 hours at room temperature and increased negligibly slowly thereafter, and azo-compounds were isolated in the yields shown, but unidentified mixtures were obtained from some other amines.

Although hydrazobenzene was almost quantitatively converted into azobenzene, no identifiable oxidation product was obtained from aniline but only a little acetanilide. It is not the reaction of acetanilide that is here being observed, however, since this is much slower than that of aniline (cf. Barlin and Riggs, following paper). In acetic acid solution at least, aniline is not initially oxidised to hydrazobenzene in the manner postulated by Pausacker (*J.*, 1953, 107). On the other hand, the negatively substituted amines examined (except 2 : 4-dinitroaniline, which consumed no reagent, and 2-nitro-1-naphthylamine, which gave an unidentified mixture of products) gave good yields of the azo-compounds, and furazan oxides were not obtained from *o*-nitro-amines (cf. Part II): this difference from the results in benzene solution recalls the experience of Green and Rowe (*J.*, 1912, **101**, 2449, 2455) who obtained benzofurazan oxide from *o*-nitroaniline and alkaline hypochlorite, but 2 : 2′-dinitroazobenzene by means of the neutral reagent. The possibility that in acetic acid there is interference with the internal hydrogen bonding of *o*-nitro-amines will be discussed in a later paper.

β-Naphthylamine gave an unexpected result. Although variable quantities of a green, high-melting compound, apparently identical with that of Part II, were obtained in different experiments, no 1 : 2 : 6 : 7-dibenzophenazine was isolated. The principal products were 2-acetamido-1 : 4-naphthaquinone (up to 34%) and a compound, $C_{22}H_{18}O_2N_2$ (25%), which is probably a β-naphthylamine anil of the quinone. When boiled with dilute hydrochloric acid the second compound yielded some β-naphthylamine and *ca.* 50% of 2-β-naphthylamino-1 : 4-naphthaquinone which was synthesised for comparison. The latter product could arise by hydrolysis of the anil and nucleophilic displacement of the acetamido-group (or the amino-group produced from it by hydrolysis) by β-naphthylamine—this displacement was substantiated by experiment. Under certain conditions the oxidation product, at first obtained in red plates, crystallised in purple needles of the same m. p., a mixture showing no depression. Since the amino-group of 2-amino-1 : 4-naphthaquinone is amidic and unlikely to be acetylated by acetic acid, and phenyl iodosoacetate cannot function as an acetylating agent, the 2-acetamido-1 : 4-naphthaquinone probably arises from the oxidation of aceto-β-naphthalide formed *in situ*; the naphthalide is indeed oxidised by phenyl iodosoacetate to the quinone in good yield but the quinone anil is not produced (Barlin and Riggs, *loc. cit.*). Since the anil is not formed from the quinone and β-naphthylamine in cold glacial acetic acid, and in view of the *meta*-acetoxylation reaction described by Barlin and Riggs, it is probable that an acetoxyl group enters the 4-position and a β-naphthyl-

* Part II, *J.*, 1953, 1989.

amino-group the 1-position, subsequent oxidation to the quinone anil occurring. On this basis the product is 2-acetamido-1 : 4-naphthaquinone 1-β-naphthylimide.

Experimental

Analyses are by Dr. K. W. Zimmermann, C.S.I.R.O. Microanalytical Laboratory, Melbourne. Samples were dried at 100°/0·5 mm. for analysis. The acetic acid used was purified (Orton and Bradfield, *J.*, 1927, 983) and had m. p. 16·3°. Ultra-violet spectra were measured in 95% alcohol on a Hilger Uvispek spectrophotometer.

Quantitative experiments were conducted as described in Part II, with acetic acid (25 ml.) in place of the benzene. A control solution showed a negligible drop in titre.

For the isolation of the products the amine (1 g.) in a little acetic acid was treated with the required amount of phenyl iodosoacetate in acetic acid (20 ml. per g.). After the required time at room temperature the mixture was evaporated as far as possible at the water-pump at <40°, and the residue was evaporated with water and alcohol under reduced pressure until free from acetic acid and iodobenzene. The residue, dried by evaporation with benzene, was extracted successively with boiling benzene and chloroform, and the cold concentrated extracts were chromatographed successively on alumina (British Drug Houses; 20 g. per g. of amine) with the same solvents as eluting media. Azo-compounds when produced were in the first benzene band, and were identified by mixed m. p. with the samples prepared in Part II, or by analyses, as shown in the Table. Acetanilide, m. p. and mixed m. p. 114°, was obtained by crystallisation from dilute alcohol of the residue from this band from the oxidation of aniline; *o*-toluidine gave a trace of white crystals, m. p. 75° from benzene–light petroleum (b. p. 60—70°); *p*-toluidine gave a few red needles, m. p. 165—167° from light petroleum (b. p. 70—80°).

Unidentified mixtures were obtained, with consumption (mols.) of iodosoacetate as stated, from: aniline 2·2, *o*- 2·0, *m*- 2·3, and *p*-toluidine 1·5, mesidine 1·3, α-naphthylamine 2·2, and 2-nitro-1-naphthylamine 2·0.

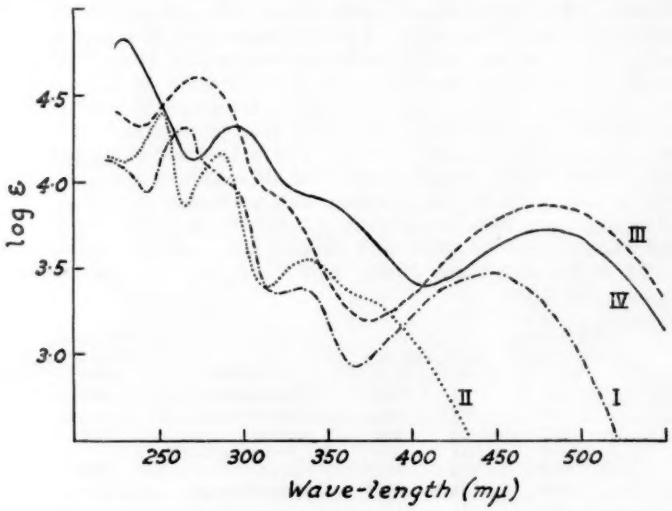
Amine	$PhI(OAc)_2$ consumed (mol.)	Azo-compound Yield (%)	M. p.*
o-Anisidine	1·9	1	153°
p- ,,	1·9	4	162
o-Chloroaniline	2·1	25	135
m- ,,	1·5	34	101
p- ,,	2·2 [a]	24	186 [b]
o-Nitroaniline	0·9	23 [c]	216 [d]
m- ,,	1·1	61	150
p-Nitroaniline	0·5 [e]	63	224°
4-Chloro-2-nitroaniline	0·2 [f]	32	251 [g]
1-Nitro-2-naphthylamine	0·8	38	315 [j]
Hydrazobenzene	1·1	97	68

* Mixed m. p.s were the same within 2° for known products.

[a] Increased to 3·0 in 6 days. [b] Sample prepared in Part II had m. p. 184°. [c] *o*-Nitroaniline (17%) was recovered. [d] An authentic sample (Green and Rowe, *loc. cit.*), crystallised from alcohol, had m. p. 196°, raised by chromatography on alumina from benzene and further crystallisation to 215°. In our hands, hypochlorite rendered neutral to phenolphthalein with acetic acid produced a little benzofurazan oxide which was removed by steam-distillation. Found, for azo-compound from iodosoacetate oxidation: C, 53·5; H, 3·2; N, 20·7. Calc. for $C_{12}H_8O_4N_4$: C, 52·9; H, 3·0; N, 20·6%. [e] Increased to 1·1 in 5 days. [f] Increased to 1·5 in 7 days. [g] 4 : 4′-*Dichloro*-2 : 2′-*dinitroazobenzene*, red needles from benzene [Found: C, 42·3; H, 1·9; N, 15·9%; *M* (Rast), 303. $C_{12}H_6O_4N_4Cl_2$ requires C, 42·3; H, 1·8; N, 16·4%; *M*, 341]. [h] Increased to 1·4 in 7 days. [j] 1 : 1′-*Dinitro*-2 : 2′-*azonaphthalene*, yellow needles from benzene (Found: C, 65·0; H, 3·4; N, 15·0. $C_{20}H_{12}O_4N_4$ requires C, 64·5; H, 3·3; N, 15·0%).

Oxidation of β-*Naphthylamine.*—β-Naphthylamine (10 g.) in a little acetic acid was treated with phenyl iodosoacetate (54 g.) in acetic acid (750 ml.). After 20 hr. at room temperature the mixture was evaporated as above. The residue was dried by distillation with chloroform, a trace only of a dark green substance being undissolved. A chloroform extract was chromatographed on alumina (150 g.). Almost the whole of the starting material was accounted for in the first (red) band, later fractions giving no crystalline products. The material from this band (9·4 g.) dissolved partly in cold benzene, and the sparingly soluble residue (2·8 g.) crystallised from alcohol in yellow plates, m. p. 206° [Found: C, 67·2; H, 4·3; N, 6·6%; *M* (cryoscopic in nitrobenzene), 212. Calc. for $C_{12}H_9O_3N$: C, 67·0; H, 4·2; N, 6·5%; *M*, 215]. The m. p. was undepressed in admixture with 2-acetamido-1 : 4-naphthaquinone, and the product was hydrolysed by concentrated sulphuric acid (Fieser, " Experiments in Organic Chemistry," Heath. New York, 2nd edn., 1941, p. 288) to 2-amino-1 : 4-naphthaquinone, m. p. and mixed m. p. 206° (from alcohol).

The benzene-soluble material was rechromatographed on alumina (50 g.) from benzene and yielded a red band followed by a yellow band from which more (0·6 g.) 2-acetamido-1 : 4-naphthaquinone was isolated. The residue from the last portion of the red band yielded a trace of purple material, m. p. at least 234—238° (from ethyl acetate), which was not further examined. The residue (3·5 g.) from the remainder of the red band was rechromatographed on alumina from benzene, the initial clear red eluate being collected in four fractions, each of which yielded red plates or purple needles, m. p. 210—211°, on crystallisation from alcohol; a mixture of the two forms also had m. p. 210—211° (yield, 2·5 g.). Recrystallisation of the red plates from a warm concentrated solution in alcohol yielded the purple needles, and these were reconverted into the red plates by slower crystallisation from a more dilute solution in the cold. *2-Acetamido-1 : 4-naphthaquinone β-naphthylimide* separated from methanol as red plates, m. p. 210—212° [Found : C, 77·5, 77·8; H, 5·1, 4·8; N, 8·1, 8·3%; *M* (Rast), 358. $C_{22}H_{16}O_2N_2$ requires C, 77·6; H, 4·7; N, 8·2%; *M*, 338].



I, 2-*Amino*-1 : 4-*naphthaquinone*.
II, 2-*Acetamido*-1 : 4-*naphthaquinone*.
III, 2-β-*Naphthylamino*-1 : 4-*naphthaquinone*.
IV, 2-*Acetamido*-1 : 4-*naphthaquinone β-naphthylimide* (*both forms*).
(*All curves determined in* 95% *alcohol.*)

In another experiment the quinone was obtained in 6% yield, the red plates in 25% yield, and the green compound in 14% yield. The last was insoluble in most of the common solvents, but formed a deep blue solution in nitrobenzene from which it separated in lustrous leaflets, m. p. >300° (cf. Part II). Absorption spectra are recorded in the Figure.

Hydrolysis of the Red Plates.—The compound (100 mg.) was refluxed with 2N-hydrochloric acid (10 ml.) for 2 hr. The scarlet needles (50 mg.) that separated were recrystallised from methanol and had m. p. 194°, undepressed in admixture with 2-β-*naphthylamino*-1 : 4-*naphthaquinone* prepared as below [Found : C, 79·9, 80·3; H, 4·4, 4·4; N, 4·6, 4·7%; *M* (Rast), 274. $C_{20}H_{13}O_2N$ requires C, 80·3; H, 4·4; N, 4·7%; *M*, 299]. The filtrate from the hydrolysis was concentrated to small bulk and cooled. The pink flakes (30 mg.) that separated had m. p. *ca.* 250° (decomp.) and were converted by benzoyl chloride and alkali into benzo-β-naphthalide, m. p. and mixed m. p. 158°.

2-β-*Naphthylamino*-1 : 4-*naphthaquinone*.—(*a*) 1 : 4-Naphthaquinone (500 mg.) and β-naphthylamine (500 mg.) were refluxed together in alcohol (10 ml.) for 2 hr. The dark product was chromatographed on alumina (10 g.) from benzene, the deep red eluate evaporated, and the residue (600 mg.) crystallised from methanol to give scarlet needles, m. p. 194° (Found : C, 80·1; H, 4·2; N, 5·1%).

(*b*) 2-Acetamido-1 : 4-naphthaquinone (63 mg.) and β-naphthylamine (60 mg.) were refluxed

in 2N-hydrochloric acid (10 ml.) for 2 hr. The red solid was chromatographed as above to yield scarlet needles, m. p. 194° from methanol, undepressed in admixture with the above product.

Attempt to Prepare a β-*Naphthylamine Anil of* 2-*Acetamido*-1 : 4-*naphthaquinone.*—The quinone (79 mg.) and β-naphthylamine (101 mg.) were shaken with glacial acetic acid (10 ml.) until dissolved. After 24 hr. the reddish solution was evaporated to dryness at the water pump and the residue treated with alcohol (10 ml.). The bright yellow residue had m. p. 206° and was clearly not the desired product. Chromatography of the total product on alumina from benzene gave an initial pink fraction from which a few colourless crystals, m. p. 108° [from light petroleum (b. p. 70—60°)], probably β-naphthylamine, were obtained.

We acknowledge financial assistance for chemicals and equipment from the Research Grant to the New England University College.

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The Reaction of Phenyl Iodosoacetate with N-*Arylacetamides.*

By G. B. BARLIN and N. V. RIGGS.

[Reprint Order No. 5256.]

Acetanilide and certain derivatives, especially those containing negative substituents, do not react appreciably with phenyl iodosoacetate at room temperature, but those containing electron-releasing substituents in the *p*-position give high yields of *m*-acetoxy-derivatives. Quinonoid products are obtained from other *N*-arylacetamides. The mechanism of the acetoxylation is discussed.

IN the preceding paper it was shown that β-naphthylamine and phenyl iodosoacetate in acetic acid gave mainly 2-acetamido-1 : 4-naphthaquinone and a compound, $C_{22}H_{16}O_2N_2$, believed to be a β-naphthylanil of the quinone, probably by way of aceto-β-naphthalide which indeed with phenyl iodosoacetate in acetic acid produces the quinone in good yield, but not the supposed anil. Reaction also occurs in benzene but much more slowly (see the Table), and the yield of quinone is lower.

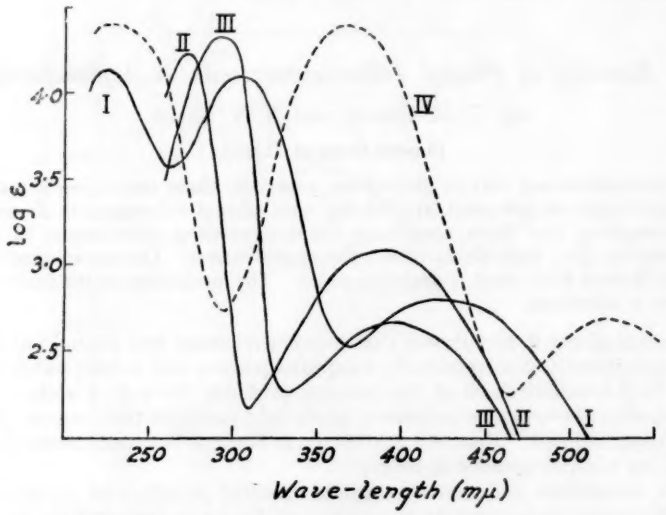
Although acetanilide and aceto-*m*-toluidide reacted slowly, and aceto-α-naphthalide rapidly, with phenyl iodosoacetate in acetic acid at room temperature, no identifiable products were obtained. The negatively substituted chloro- and nitro-acetanilides reacted negligibly slowly, but other *N*-arylacetamides readily. The Table shows the uptakes of reagent, determined by Pausacker's method (*J.*, 1953, 1989), which are some measure of the relative speeds of reaction; comparative results for benzene solution for some of the more reactive compounds are also given. No absolute significance is attached to the uptakes which increase slowly for several days.

Acetyl derivative of	$PhI(OAc)_2$ consumed (mol.) In AcOH 24 hr.	In AcOH 4 days	In C_6H_6 24 hr.	In C_6H_6 4 days	Acetyl derivative of	$PhI(OAc)_2$ consumed (mol.) In AcOH 24 hr.	In AcOH 4 days	In C_6H_6 24 hr.	In C_6H_6 4 days
Aniline	0·0	0·2	—	—	*o*-Anisidine	1·9	2·4	—	—
o-Toluidine	1·4	1·9	0·0	0·0	*p*- ,, ...	2·0	2·5	0·1	0·2
m- ,, ...	0·0	0·3	—	—	*p*-Phenetidine ...	1·9	2·5	—	—
p- ,, ...	1·2	1·6	0·3	0·5	α-Naphthylamine	2·2	2·6	—	—
Mesidine	2·4	2·7	—	—	β- ,,	2·2	2·3	0·5	1·3

Aceto-*p*-toluidide, aceto-*p*-anisidide, and phenacetin underwent acetoxylation in a position *meta* to the acetamido-group, yields being good. The orientation was unexpected, and the product from aceto-*p*-toluidide was rigorously identified to prove it. Sandin and McCormack (*J. Amer. Chem. Soc.*, 1945, **67**, 2051) found phenyl iodosoacetate to be a methylating agent toward trinitrotoluene, as is also lead tetra-acetate (Fieser, Clapp, and Daudt, *ibid.*, 1942, **64**, 2052) which, at lower temperatures, acetoxylates reactive aromatic hydrocarbons (Fieser *et al.*, *ibid.*, 1938, **60**, 2542, 1893; 1940, **62**, 432). No record of Sandin's proposed investigation of phenyl iodosoacetate as an acetoxylating agent (*Chem.*

Reviews, 1943, **32**, 260) has been found, and the present work seems to be the first report of its efficacy in this respect toward the aromatic nucleus, although Criegee and Beucker (*Annalen*, 1939, **541**, 218) found that it converted unsaturated compounds into glycol diacetates.

Traces of yellow products were obtained in the reactions with aceto-*p*-toluidide and phenacetin, and the method of preparation and analyses suggest that these are 2-acetamido-5-methyl- and -5-ethoxy-*p*-benzoquinone, respectively. In confirmation, the ultra-violet absorption spectra (see Figure) resemble closely that of 2 : 5-bisdimethylamino-*p*-benzoquinone (Braude, *J.*, 1945, 490) displaced somewhat to shorter wave-lengths. Aceto-*o*-anisidide gave a moderate yield of an orange compound, $C_{11}H_{13}O_4N$ (which, for the above reasons, is probably 2-acetamido-3-methoxy-*p*-benzoquinone), and a colourless substance which gave analyses corresponding to those of an acetoxy-derivative of aceto-*o*-anisidide



I, 2-*Acetamido*-3-*methoxy*-p-*benzoquinone*.
II, 2-*Acetamido*-5-*methyl*-p-*benzoquinone*.
III, 2-*Acetamido*-5-*ethoxy*-p-*benzoquinone*.
IV, 2 : 5-*Bisdimethylamino*-p-*benzoquinone* (*redrawn from Braude*, loc. cit.).
Curve I determined in 95% EtOH, *the others in* $CHCl_3$.

but appeared to give a mixture on hydrolysis and subsequent methylation. By contrast, aceto-*o*-toluidide yielded no acetoxylation product, and the acetamido-group was not present in the quinonoid product, toluquinone.

Although the products from the reaction in benzene were examined only with aceto-β-naphthalide, the much greater rates of reaction and especially the formation of high yields of acetoxylation products from appropriate compounds in the polar solvent, acetic acid, may indicate that acetoxylation proceeds by an ionic rather than by a radical mechanism such as that postulated by Pausacker (*J.*, 1953, 107) for the conversion of amines into azo-compounds. In any case the initial stages cannot generally involve the acetamido-group for, if this group were attacked homolytically, nucleophilically, or electrophilically, the necessary reactivity for acetoxylation could be developed only in the *o*- or *p*-position, as is soon shown by a consideration of possible contributors to the respective hybrid intermediate structures. Since the acetamido-group alone does not produce the necessary activation and electron-attracting groups inhibit the reaction entirely, electrophilic substitution in a position *ortho* to an electron-releasing group such as methyl or alkoxyl seems the most likely mechanism. In partial confirmation, acetomesidide, with two positions *meta* to the

acetamido-group highly activated to electrophilic attack, gave a good yield of a product that gave correct analyses for the expected diacetoxy-derivative except that hydrolyses with 50% sulphuric acid gave only 2·5 equivalents of acetic acid.

The mechanism of the acetoxylation is being investigated.

Experimental

For general notes see the preceding paper.

Oxidation of Aceto-β-naphthalide.—(a) *In acetic acid.* Aceto-β-naphthalide (2 g.) in a little acetic acid was added to a solution of phenyl iodosoacetate (7·9 g.) in acetic acid (160 ml.). After 14 hr. at room temperature the mixture was evaporated as described in the preceding paper. Chromatography of a chloroform extract of the dry residue on alumina (60 g.) gave successively reddish-green (25 ml.), yellowish-green (80 ml.), and bright green (160 ml.) fractions; later fractions gave negligible residues. The material from the first two fractions crystallised from acetone as yellow plates (850 mg.), m. p. 206°, undepressed in admixture with 2-acetamido-1 : 4-naphthaquinone. The reddish-green filtrate combined with the third fraction yielded green needles (40 mg.), m. p. >300°, readily soluble in hot acetone, but not further investigated. No crystalline material was obtained from the mother-liquors.

(b) *In benzene.* After 4 days at room temperature the reaction in this solvent gave 11% of the quinone as the only crystalline product.

Unsuccessful Oxidations.—Starting material (55%) was the only crystalline fraction obtained from acetanilide after 5 days' treatment with the reagent in acetic acid at 30° or (40%) from aceto-*m*-toluidide after 21 days. Aceto-α-naphthalide yielded only a series of gums after 24 hr.

Acetoxylation of Aceto-p-toluidide.—Aceto-*p*-toluidide (1 g.) was kept with phenyl iodosoacetate (3 g.) in acetic acid (100 ml.) for 24 hr. at room temperature, then worked up as usual. Chromatography on alumina (20 g.) from chloroform gave a yellow fraction the material from which (*ca.* 1 g.) was rechromatographed on alumina (30 g.) from benzene. The first (yellow) band gave a trace (10 mg.) of 2-*acetamido*-5-*methyl*-p-*benzoquinone*, yellow needles that sublimed readily at 130—140°/0·5 mm. and then had m. p. 175° (Found : N, 7·5. $C_9H_9O_3N$ requires N, 7·8%). The bulk of the product was in the succeeding pale yellow band which gave colourless crystals, m. p. 132° from benzene–light petroleum (b. p. 70—80°), raised by sublimation at 125°/0·5 mm. to 133·5°, undepressed on admixture with 4-acetamido-2-acetoxytoluene.

This product (120 mg.) was dissolved in methanol (5 ml.), 10% aqueous sodium hydroxide (5 ml.) added, and the methanol boiled off on the water-bath. The mixture was acidified with 10N-hydrochloric acid and chilled. The white solid (40 mg.) was collected and, sublimed at 215°/0·5 mm., had m. p. 224°, undepressed on admixture with 4-acetamido-2-hydroxytoluene.

Three treatments of the acetoxy-compound in a little methanol with methyl sulphate (0·5 ml.) and 10% sodium hydroxide, extraction with chloroform, and crystallisation of the residue from benzene–light petroleum (b. p. 70—80°) gave colourless needles, m. p. 132°, undepressed in admixture with 4-acetamido-2-methoxytoluene.

Acetoxylation of Aceto-p-anisidide and Phenacetin.—Aceto-*p*-anisidide (5 g.), treated and worked up as for aceto-*p*-toluidide, gave 4-acetamido-2-acetoxyanisole (4·95 g.), m. p. 158° from benzene–light petroleum (b. p. 60—70°) (Found : C, 59·7; H, 5·3; N, 6·4. Calc. for $C_{11}H_{13}O_4N$: C, 59·2; H, 5·8; N, 6·3%). The product was converted by methyl sulphate and alkali into 4-acetamidoveratrole, m. p. and mixed m. p. 132° from benzene–light petroleum (b. p. 70—80°). Phenacetin (2 g.) gave a trace (80 mg.) of 2-*acetamido*-5-*ethoxy*-p-*benzoquinone*, yellow needles, m. p. 216° from benzene–light petroleum (b. p. 70—80°), and subliming readily at 217° (Found : N, 7·2; OEt, 21·4. $C_8H_6O_3N{\cdot}OC_2H_5$ requires N, 6·7; OEt, 21·5%). The main product was 4-acetamido-2-acetoxyphenetole (1·55 g.), m. p. 134° after sublimation at 160°/0·5 mm. and recrystallisation from benzene–light petroleum (b. p. 70—80°) (Found : C, 61·2; H, 6·2; N, 6·2. Calc. for $C_{12}H_{15}O_4N$: C, 60·8; H, 6·4; N, 5·9%). Hydrolysis and methylation as above gave 4-acetamido-2-methoxyphenetole, m. p. 143° from benzene–light petroleum (b. p. 70—80°). Hydrolysis and ethylation with sodium hydroxide and ethyl sulphate gave 4-acetamidocatechol diethyl ether, m. p. 126° from benzene–light petroleum (b. p. 70—80°).

Oxidation of Aceto-o-toluidide.—Aceto-*o*-toluidide (2 g.) was oxidised with phenyl iodosoacetate (8·6 g.) in acetic acid (130 ml.) for 7 days at room temperature. Evaporation at the water-pump gave a yellow distillate, and steam-distillation of the residue gave a yellow crystalline solid. The combined distillates and solid were extracted with ether which was then washed with sodium carbonate solution, dried (Na_2SO_4), and evaporated. The yellow solid residue

sublimed readily from the water-bath and then had m. p. 67—68°, undepressed in admixture with *o*-toluquinone. The residue from the steam-distillation was chromatographed on alumina (40 g.) from chloroform and yielded starting material (470 mg.), m. p. and mixed m. p. 108° from light petroleum (b. p. 60—70°).

In another experiment the quinone was steam-distilled and the total distillate saturated with sulphur dioxide. Solvents were evaporated at the water-pump and the oily residue extracted with benzene, to give 43% of toluquinol, m. p. and mixed m. p. 124—125° from benzene.

Oxidation of Aceto-o-anisidide.—Aceto-*o*-anisidide (1·6 g.) was oxidised with phenyl iodosoacetate (6·2 g.) in acetic acid (100 ml.) for 24 hr. at room temperature and worked up as above. The residue chromatographed on alumina (30 g.) from benzene yielded a purplish-red eluate, the residue from the evaporation of which (460 mg.) gave colourless crystals of which the m. p. was raised to 165—167° by several recrystallisations from benzene–light petroleum (b. p. 70—80°), and further to 169·5—170° (softening from 165°) by sublimation at 145—150°/0·5 mm. (Found : C, 59·5; H, 5·8; N, 6·6; OMe, 13·1. $C_{10}H_{10}O_3N{\cdot}OCH_3$ requires C, 59·2; H, 5·9; N, 6·3; OMe, 13·9%). Chloroform eluted only dark material from the column. Treatment with warm aqueous-methanolic sodium hydroxide and acidification converted the above product into a black powder. Treatment with sodium hydroxide and methyl sulphate, and extraction with chloroform, gave an oil that crystallised from benzene–light petroleum (b. p. 50—60°) in pearly flakes which softened at *ca.* 90° and were completely molten only at 110°. Sublimation at 80°/0·5 mm. gave an initial fraction (<1 mg.) of fine needles, m. p. 81—81·5°, which was quickly followed by a fraction softening and melting progressively above 79°. Attempted fractional sublimation at 60°/0·005 mm. was unsuccessful.

In another experiment, aceto-*o*-anisidide (5 g.) yielded a chloroform-insoluble residue of orange solid (330 mg.) which could be satisfactorily recrystallised only from a large volume of boiling alcohol and then formed orange needles of *2-acetamido-3-methoxy-p-benzoquinone*, m. p. 253—254° (decomp.) (Found : C, 55·8; H, 4·7; N, 7·4; OMe, 15·5. $C_8H_6O_3N{\cdot}OCH_3$ requires C, 55·4; H, 4·6; N, 7·2; OMe, 15·9%). Much loss occurred on recrystallisation, as the compound was decomposed by alcohol (cf. Braude, *loc. cit.*), evaporation of a solution of the pure material yielding only a dark gum from which a few crystals slowly separated. The ultraviolet absorption spectrum was rapidly determined on a freshly prepared solution in 95% alcohol.

Acetoxylation of Acetomesidide.—Acetomesidide (1 g.) was treated with phenyl iodosoacetate (4·4 g.) in acetic acid (100 ml.). After 22 hr. at room temperature the mixture was worked up as usual. The chloroform eluate yielded colourless crystals (990 mg.), probably OO′N-*triacetyl-2 : 4 : 6-trimethylphloramine*, m. p. 244° from ethyl acetate–light petroleum (b. p. 70—80°) [Found : C, 61·8, 61·8; H, 6·5, 6·4; N, 4·9; Ac, 37·1, 37·8% after 3 times the normal period of hydrolysis with 50% sulphuric acid; *M* (Rast), 278, 303. $C_{15}H_{19}O_5N$ requires C, 61·4; H, 6·5; N, 4·8; 3Ac, 44·1%; *M*, 293].

No identifiable product was obtained from this material by means of 10% hydrochloric acid, sodium methoxide in chloroform–methanol, sodium hydroxide and methyl sulphate, benzoyl chloride and alkali, or potassium permanganate.

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Photochromism and Reversible Multiple Internal Transitions in Some spiro*Pyrans at Low Temperatures. Part II.**

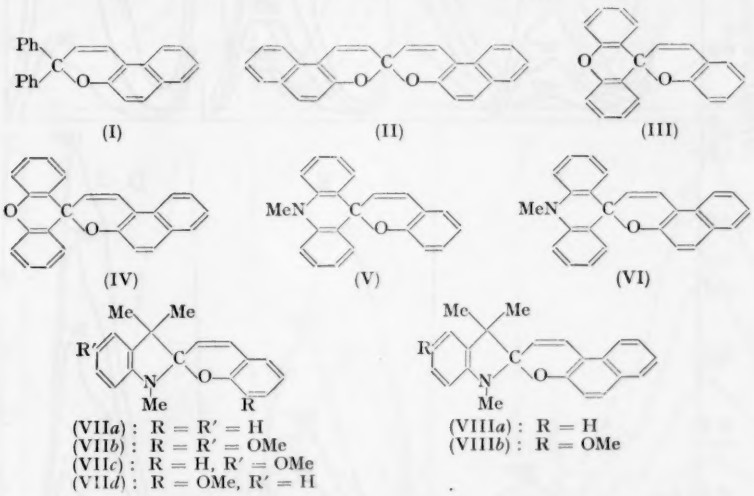
By Yehuda Hirshberg and Ernst Fischer.

[Reprint Order No. 5268.]

The investigations described in Part I were extended to additional compounds. Under appropriate conditions each photochromic compound gives rise to one or more coloured modifications, all of which spontaneously revert to the original colourless modification at rates depending on the temperature. Thermochromic and photochromic absorption spectra are recorded and compared. Heats of interconversion of coloured and colourless modifications are estimated. In several cases the colour of the dyes formed by ultra-violet irradiation at low temperatures was found to depend reversibly on the temperature of measurement.

It is tentatively suggested that the various coloured modifications in each compound are stereoisomers.

In Part I of this series * photochromism was reported and discussed for a group of *spiro*pyrans. The present paper describes an extension of this investigation to several related compounds, namely, those represented by the formulæ (I)—(VIII).



Figs. 1 and 2 show the absorption spectra, at several temperatures, of those among the above compounds which exhibit thermochromism. The increase, with temperature, of the height and area of the curves again indicates a thermal equilibrium between a coloured and a colourless modification, the latter being at a higher energy level.

A comparison of the shape and height of the curves obtained for each compound in various solvents shows that (*a*) polar solvents shift the equilibrium in favour of the dye, and (*b*) in several cases the ratio between the heights of two peaks depends greatly on the solvent. Thus compound (VIII*a*) in dimethyl phthalate has a pronounced peak at 565 mμ and a smaller one at 540 mμ, whereas in diphenyl ether peaks of about equal height are found at 560 and 530 mμ and in decalin there is a shoulder at 555 and a peak at 520 mμ. Compound (VIII*b*) behaves similarly. With other compounds, only shifts towards shorter wavelengths were observed on passing from polar to non-polar solvents : however, these may

* Part I, *J.*, 1954, 297.

also be due to a change in the ratio between two overlapping peaks. Some compounds show rather broad absorption bands and pronounced shoulders, indicating the co-existence

FIG. 1. *Absorption spectra of thermochromic compounds at several temperatures in dimethyl phthalate* (d.m.p.), *diphenyl ether* (d.p.e.) *or decalin* (d.).

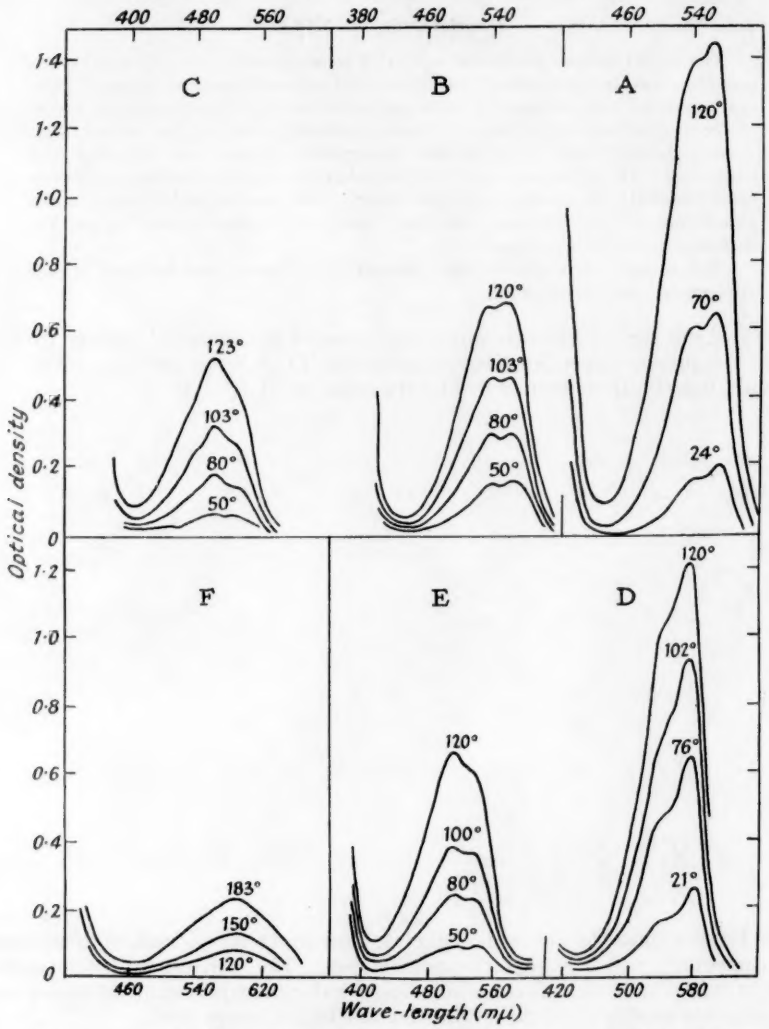


Fig.	Substance	Solvent	Concn. (g./l.)	Fig.	Substance	Solvent	Concn. (g./l.)
1*A*	(VIII*a*)	d.m.p.	1·4	1*D*	(VIII*b*)	d.m.p.	1·0
1*B*	,,	d.p.e.	1·4	1*E*	,,	d.	3·0
1*C*	,,	d.	3·7	1*F*	(VII*c*)	d.m.p.	3·0

of more than one coloured species [cf. compound (II)]. This assumption is supported by the photochromic absorption spectra described further on.

Compounds (VII*a* and *b*) are not thermochromic, but heating to about 130° irreversibly converts them into dyes, the absorption spectra of which are somewhat similar to those of the related compound (VIII*b*) (Fig. 2).

The possible overlapping, in the observed absorption spectra, of several bands which may differ with regard to their dependence on temperature, makes it impossible to evaluate exactly the heat of conversion, ΔH, between coloured and colourless modifications from the

FIG. 2. *Absorption spectra of thermochromic compounds at several temperatures in dimethyl phthalate* (d.m.p.), *diphenyl ether* (d.p.e.) *or decalin* (d.).

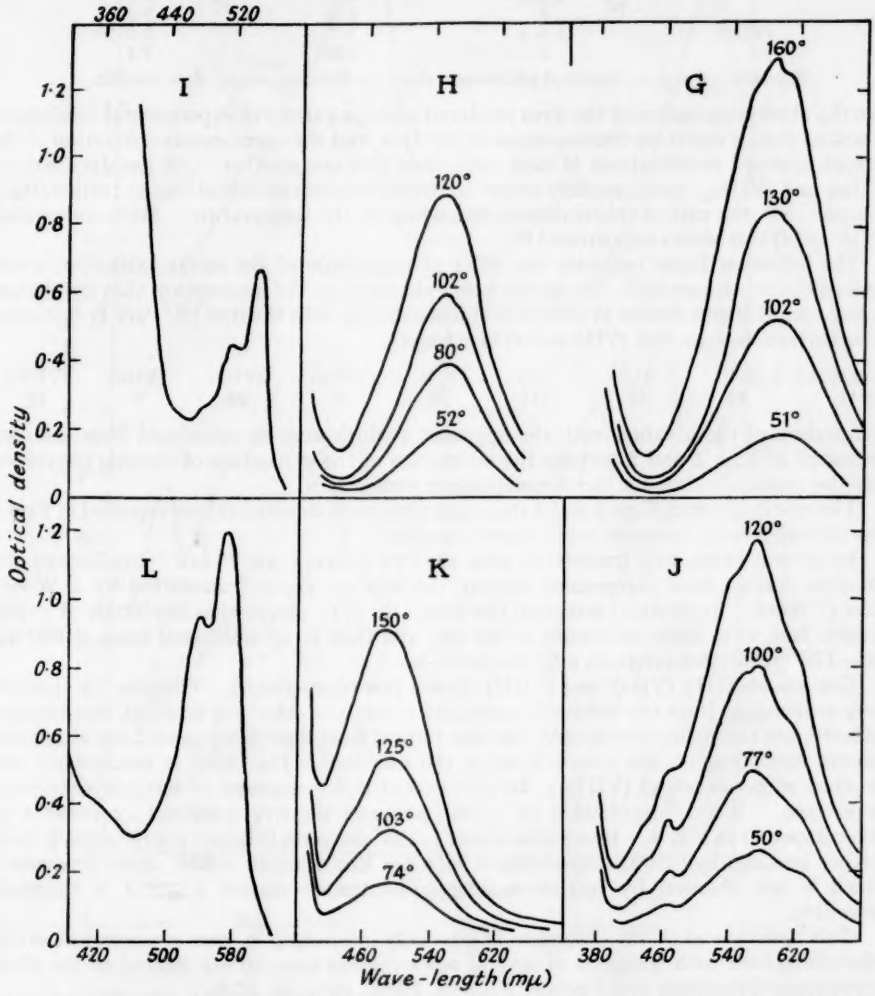


Fig.	Substance	Solvent	Concn. (g./l.)	Fig.	Substance	Solvent	Concn. (g./l.)
2*G*	(VI)	d.m.p.	0·4	2*J*	(II)	d.m.p.	1·2
2*H*	,,	d.	1·0	2*K*	(IV)	,,	3·5
2*I*	(VII*a*)	d.m.p.	3·0	2*L*	(VII*b*)	d.p.e.	1·3

curves given in Figs. 1 and 2. The values summarized in the following Table should therefore be regarded only as approximations. They were calculated from the rectilinear plots of log (maximal extinction coefficient) against the reciprocal of the absolute temperature.

All the compounds examined, except (I), (V), and (VII*a*), exhibit pronounced photochromism, *i.e.*, when their solutions are irradiated with ultra-violet light at low temperatures very intensely coloured dyes are reversibly developed. Figs. 3 and 4 (and their legends)

Compound	Solvent	$\lambda_{max.}$ (mμ)	ΔH (kcal./mole)
(II)	d.m.p.	580	5·3
(IV)	,,	495	6·4
(VI)	,,	590	5·1
(VI)	d.	560	5·5
(VII*c*)	d.m.p.	580	7·0
(VIII*a*)	,,	565	4·9
	d.p.e.	560	5·4
	d.	520	7·2
(VIII*b*)	d.m.p.	575	3·5
	d.	530	7·4

Solvents: d.m.p. = dimethyl phthalate; d.p.e. = diphenyl ether; d. = decalin.

give the absorption curves of the dyes produced under a variety of experimental conditions, as well as details about the luminescence of the dyes, and the spontaneous conversion of the various coloured modifications of each compound into one another. All the dyes, except $(VII b)_2$ and $(VII d)_2$, spontaneously revert to their colourless modifications at temperatures around −50°, the rate of this reversion depending on the temperature. With compounds (VII*b* and *d*) this occurs only around 0°.

The following Table indicates the order of magnitude of the molar extinction coefficients ε of the various dyes, the figures being obtained on the assumption that irradiation at low temperatures results in complete transformation into the dye (cf. Part I) [solutions in methyl*cyclo*hexane, but (VII*b* and *d*) in ethanol]:

Compound	(II)	(III)	(IV)	(VI)	(VII*b*)	(VII*c*)	(VII*d*)	(VIII*b*)
$10^{-3}\varepsilon$	44	21	115	30	5	23	6	46

Comparison of these values with the apparent ε which may be calculated from the data presented in Figs. 1 and 2 permits the estimation of the percentage of thermal conversion into the respective dyes for the thermochromic compounds.

The results given in Figs. 3 and 4 are in many respects similar to those reported in Part I. The following facts, however, merit special mention.

In several cases only irradiation with the full mercury arc (" full " irradiation) was effective, but in most compounds already the 365 mμ group transmitted by a Wood's filter (" Wood " irradiation) produced the dyes. In (VI), progressive irradiation at −100° results, first, in a single maximum at 560 mμ, and then in an additional band at 690 mμ. At −170° irradiation produces only the latter band.

Compounds (III), (VII*c*), and (VIII*b*) show a new phenomenon. Whereas the spontaneous conversions from one coloured modification into the other (on heating), as described hitherto, are thermally irreversible, the dyes formed from these compounds have absorption spectra depending on the temperature of the solutions. The effect is particularly pronounced with compound (VIII*b*). In solutions of this compound in methyl*cyclo*hexane–*iso*pentane, " Wood " irradiation at −180° produces the dye described by curve 1 for this compound in Fig. 4. Heating to about −135° converts this curve into curve 2, while further heating, to −100°, transforms it into 3. Recooling to −135° again produces 2, which is not changed by further cooling. The transformation $2 \rightleftarrows 3$ is thermally reversible.

This new type of thermochromism is especially interesting in view of somewhat similar effects observed with solutions of several *mero*cyanines structurally related to the above *spiro*pyrans (Hirshberg and Fischer, *J. Chem. Phys.*, 1954, **22**, 572).

Compounds (VII*b* and *d*) exhibit photochromism only when dissolved in alcohol, and not in methyl*cyclo*hexane, possibly because of an interaction between solute and solvent.

Comparison of Figs. 1 and 2 with Figs. 3 and 4 shows that in general those dyes which are formed thermally at elevated temperatures correspond to the dyes which are produced from the same compounds by ultra-violet irradiation at about −100°, or by irradiation at still lower temperatures followed by heating to about −100°.

Some of the maxima at longer wave-lengths in the photochromic absorption curves also appear, at least as shoulders, in the thermochromic spectra. Thus, (II) in Fig. 2 shows a distinct shoulder which corresponds to the maximum at 650 mμ existing in the photochromic curve of this compound (Fig. 3). The low temperatures at which photochromic spectra are

FIG. 3. *Absorption spectra of photochromic compounds under various conditions* (in methyl*cyclo*hexane–*iso*pentane unless otherwise stated).

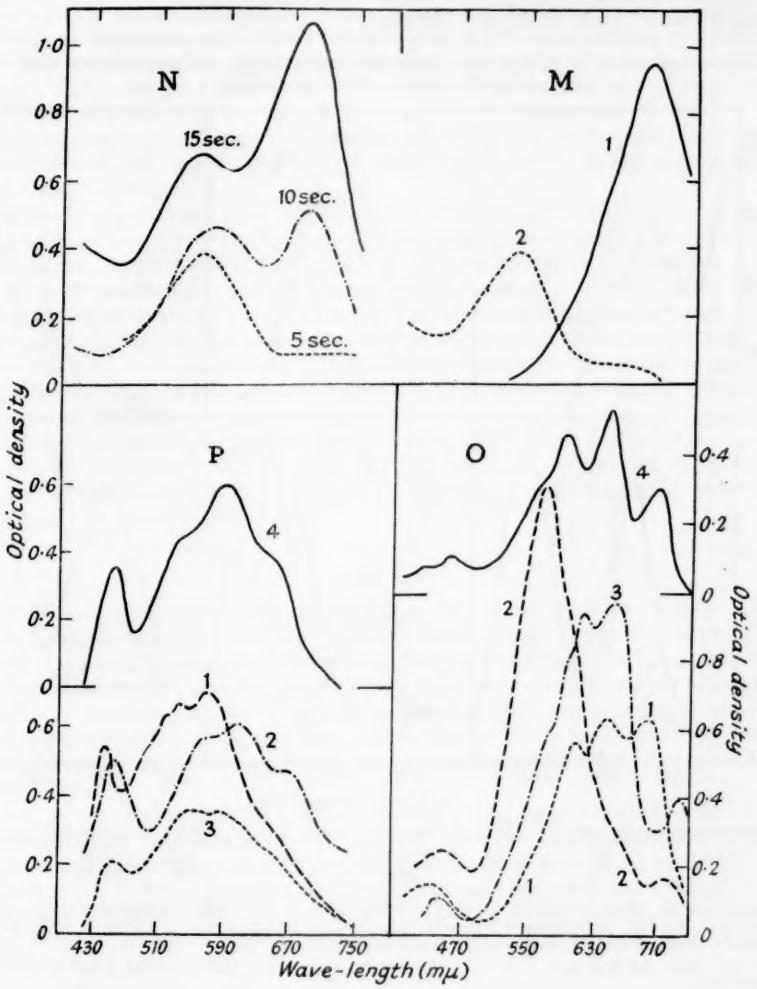


Fig.	Substance	Concn. (mg./l.)	Fig.	Substance	Concn. (mg./l.)
3*M*	(VI)	8	3*O*	(II)	8
3*N*	,,	8	3*P*	(III)	10

3*M*: curve 1, soln. after 2 min.' "Wood" irradiation at −170°; curve 2, soln. 1 heated to −135° and re-cooled (red luminescence).

3*N*: effect of progressive "Wood" irradiation at −100°; solutions were cooled to −170° after each irradiation period.

3*O*: curve 1, after 10 min. "Wood" irradiation at −170°; curve 2, soln. 1 heated to −140° and re-cooled to −170°; curve 3, soln. 2 heated to −100°, not changed when re-cooled to −170°; curve 4, soln. in ethanol–methanol after 5 min.' "Wood" irradiation at −130° (notes eparate scale). Curve 2 is also obtained by "Wood" irradiation at −140°.

3*P*: curve 1, soln. after 1 min.' "full" irradiation at −183°; curve 2, soln. 1 heated to −160° and re-cooled; curve 3, soln. 2 heated to −100°; states 2 and 3 are thermally interconvertible. Curve 4, soln. in ethanol–methanol after 1 min.' "full" irradiation at −160° (note separate scale), not changed when heated to −100°.

taken of course tend to sharpen the maxima, as compared with those measured at high temperatures. The appearance of the shoulder at 650 mμ shows that the energy level of the modification characterized by this band is not considerably higher than the modification possessing its main bands at 580 and 540 mμ.

FIG. 4. *Absorption spectra of photochromic compounds under various conditions* (in methyl*cyclo*-hexane-*iso*pentane unless otherwise stated).

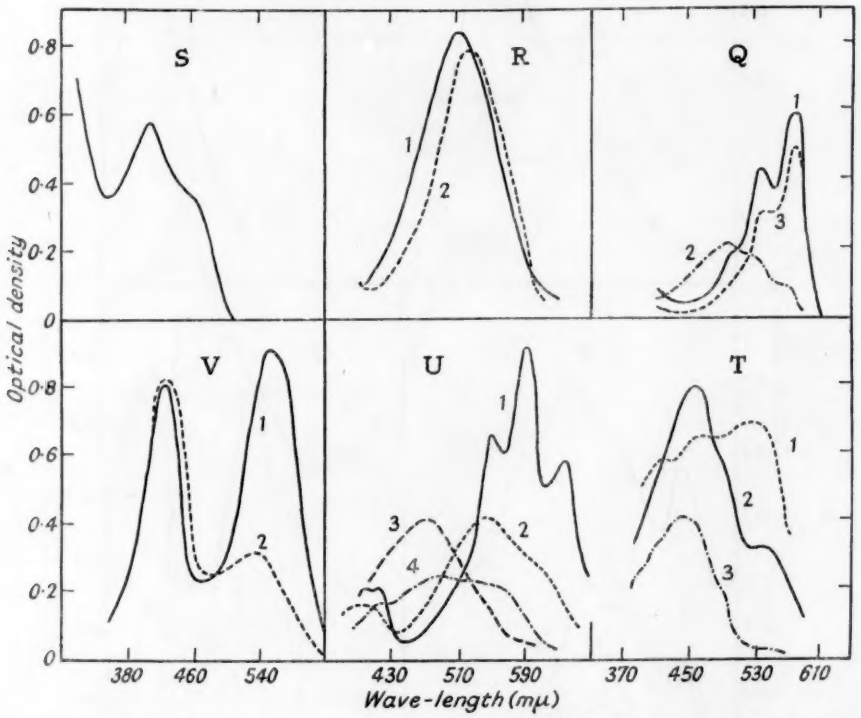


Fig.	Substance	Concn. (mg./l.)	Fig.	Substance	Concn. (mg./l.)	Fig.	Substance	Concn. (mg./l.)
4*Q*	VIII*b*)	10	4*S*	(VII*d*)	20	4*U*	(VII*c*)	15
4*R*	(IV)	1	4*T*	(VII*c*)	10	4*V*	(VII*b*)	80

4*Q*: curve 1, soln. after 15 min.' " Wood " irradiation at −180° (red luminescence); curve 2, soln. 1 heated to −135°, not changed by re-cooling (yellow luminescence); curve 3, soln. 2 heated to −100°; states 2 and 3 are thermally interconvertible.

4*R*: curve 1, soln. after 2 min.' " Wood " irradiation at −181°; curve 2, soln. 1 heated to −115° and re-cooled.

4*S*: soln. in ethanol–methanol after 5 min.' " full " irradiation at −160°. Thermal disappearance of colour starts only at about 0°.

4*T*: curve 1, soln. in ethanol–methanol after 3 min.' " full " irradiation at −150° (red luminescence), not changed when heated to −140°; curve 2, soln. 1 heated to −100° and re-cooled (yellow luminescence); curve 3, soln. 1 after 5 min.' " yellow " irradiation at −140° (yellow luminescence).

4*U*: curve 1, soln. after 10 min.' " full " irradiation at −183° (red luminescence); curve 2, soln. 1 heated to −170° (red luminescence); curve 3, soln. 2 heated to −105° (yellow luminescence); curve 4 soln. 3 heated to −70°; states 3 and 4 are thermally interconvertible.

4*V*: curve 1, soln. in ethanol–methanol after 5 min.' " full " irradiation at −150°; curve 2, soln. 1 heated to −85° and re-cooled.

Disappearance of the photochromic colours under " yellow " irradiation from a carbon arc (cf. Part I) was observed with compounds (VI), (VII*c*), and (VIII*b*). Preferential disappearance of one of two absorption bands is shown in Fig. 4 for compound (VII*c*). With the above compounds, just as with (VIII*a*) described previously, eradication of colour is much faster in alcoholic solutions.

Compound (VII*a*) is neither photochromic nor thermochromic, but shows another reversible effect of ultra-violet irradiation, analogous to photochromism. In solutions of (VII*a*) in methyl*cyclo*hexane–*iso*pentane at −183° no luminescence is excited by the 365 mμ mercury group. Irradiation with the full mercury arc at this temperature results in a strong pink luminescence, which becomes yellow when the solution is heated to about −120° and refrozen, and disappears when the solution is heated to room temperature and refrozen. This compound thus seems to be reversibly converted into a luminescent form, the existence of which does not depend on the rigidity of the solvent.

The behaviour of compound (V) is rather surprising. It differs from the related compounds (III) and (VI) in not being photochromic, and in exhibiting strong luminescence in the unirradiated state.

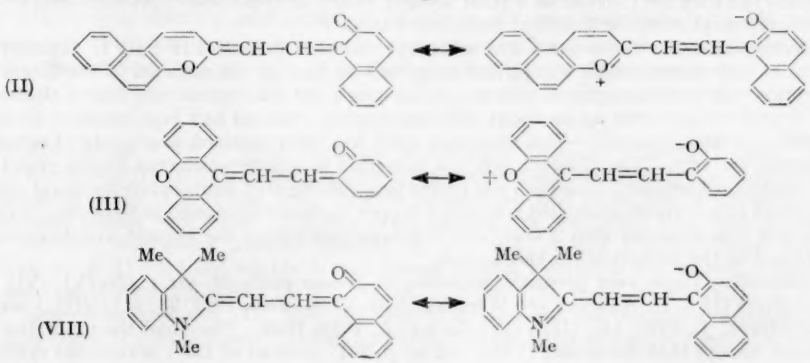
Additional experiments were undertaken to obtain direct evidence for the proposed high polarity of the dye formed on ultra-violet irradiation of compound (VIII*a*) (Fischer and Hirshberg, *J.*, 1952, 4522). Solutions of this compound at a concentration of about 1 g./l. in methyl*cyclo*hexane–decalin were irradiated between −70° and −100°, but without significant increase in the dielectric constant. No visible flocculation occurred under these conditions (cf. Part I), so that some other explanation must be sought for this observation. It should be recalled that under similar conditions solutions of the photochromic xanthylideneanthrone exhibit a pronounced increase in their dielectric constant (Hirshberg and Fischer, *J.*, 1953, 629).

It is hoped to detect the expected effect in more dilute solutions by the application of a new technique suggested by Dr. E. H. Frei of this Institute. According to his method the absorption of polarised light in the respective solutions will be measured, with the latter being placed in a strong electric field.

Discussion

The various points raised in the discussion of Part I also apply to the present investigation, and will only be outlined here. In each compound the original spiran and the dyes produced from it at progressively decreasing temperatures represent progressively higher energy levels, a few kilocalories apart from each other and separated by potential barriers of 10—20 kcal. Indirect evidence for the high polarity of the dyes is provided by the difference between solvent effects in polar and non-polar solvents, and by the large molar polarisation observed for related *mero*cyanines (Bergmann, Weizmann, and Fischer, *J. Amer. Chem. Soc.*, 1950, **72**, 5009).

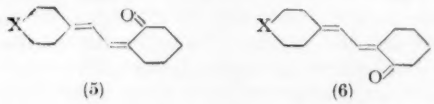
The existence of several dye modifications with each compound may be due to various electronically excited metastable states. Another tentative explanation may be that these dyes are geometrical isomers of the open, *mero*cyanine form postulated for all the coloured modifications (cf. Part I). For example, in analogy with the conclusions reached previously, the dyes corresponding to the compounds (II), (III), and (VIII) may be represented by the annexed formulæ, in which contributions of bipolar mesomers are indicated in each case :



Resonance within these conjugated systems requires a more or less planar structure for the dye molecules, in which *cis–trans*-isomerism may occur both with regard to the central " single " bond and the two adjoining " double " bonds. The " *s* "-*cis*-form is in all cases ruled out for steric reasons. The four possible isomers with respect to the two double bonds are schematically indicated in the formulæ **1**—**4** for compounds (II) and (VIII) (X stands for oxygen or nitrogen) :

(1) (3) (2) (4)

For compound (III) [and the analogous compounds (IV, V, and VI)] configurations **1** and **3**, and **2** and **4**, are identical, leaving **5** and **6** as the two possible structures :



(5) (6)

The observed differences between the absorption curves of the postulated isomers are considerably larger than those commonly encountered among geometrical isomers, and may be due to differences in both the distance between the heteroatoms and the contribution of the two main mesomers, among at least some of the isomers of each compound. In accordance with the above reasoning less coloured isomers were found for compounds related to (III) than for those related to (II) and (VII). The low bond order of the two central " double " bonds may explain the easy spontaneous transformations of the isomers.

Coenen and Pestemer in a recent paper (*Z. Elektrochem.*, 1953, **57**, 785) report the isolation of several pairs of *cis–trans*-isomers in somewhat related *mero*cyanines. They found no significant difference between the absorption spectra of the isomers and concluded that the heteroatoms at both ends of the conjugated system do not participate in this conjugation. The present investigation shows that the situation is probably different in the compounds described here.

The existence of stereoisomers in symmetrical cyanine dyes has been assumed by H. Kuhn (*Helv. Chim. Acta*, 1951, **34**, 1308) and supported experimentally by Zechmeister and Pinckard (*Experientia*, 1953, **9**, 16).

Experimental

Solvents.—For work at low temperature a nonpolar solvent mixture of equal parts (by vol.) of methyl*cyclo*hexane and *iso*pentane was used. Both solvents were purified by treatment with sulphuric acid and passage through a column of activated silica gel. A mixture of ethanol and methanol (4 : 1 by vol.) served as a polar solvent at low temperatures. At high temperatures decalin, diphenyl ether, or dimethyl phthalate was used.

Spectrophotometric Technique.—The technique was that described in Part I. Temperature control at high temperatures was further simplified by heating the contents of the Dewar-type absorption cells used throughout, with air passing over a coil of nichrome wire heated electrically. Any desired temperature up to about 180° was rapidly attained and kept constant within 1°.

Dielectric Measurements.—The technique used has been outlined previously (Fischer and Hirshberg, *loc. cit.*). The dielectric cell was immersed in a large unsilvered Dewar vessel filled with methyl*cyclo*hexane. This bath was cooled below the desired temperature by liquid nitrogen introduced at a variable controlled rate into a copper container immersed in the bath. Thermoregulation was achieved with a bimetallic regulator controlling the current in a bare heating coil placed at the bottom of the thermostat.

Materials.—These were prepared according to known methods, viz. : (I), (V), (VI), (VII *a*, *b*, *c*, *d*), (VIII *a*, *b*), Wizinger and Wenning, *Helv. Chim. Acta*, 1940, **23**, 247; (II), Dickinson and Heilbron, *J.*, 1927, **14**; (III), (IV), Irving, *J.*, 1929, 1093. They had the properties there recorded, except that compound (VII*d*) had m. p. 201° (instead of 122°) in repeated syntheses;

the compound showed the colour reactions described by the above authors; the figure 122° may therefore be a misprint.

The authors are deeply indebted to Prof. Linus Pauling for helpful advice, and to Mr. M. Kaganowitch for the preparation of all the compounds investigated.

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REHOVOTH, ISRAEL. [*Received, March 31st*, 1954.]

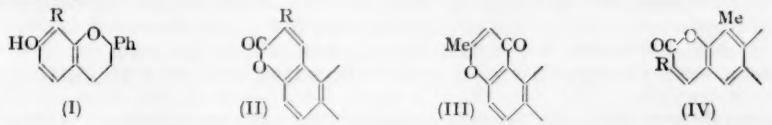
The Pigments of "Dragon's Blood" Resin. Part V. Some Flavans.*

By ALEXANDER ROBERTSON, V. VENKATESWARLU, and W. B. WHALLEY.

[Reprint Order No. 5249.]

The method developed in Part III (*J.*, 1950, 3117) has been extended to the synthesis of flavans and their derivatives from a series of polyhydroxyphenols. From some a number of α- and γ-pyronoflavans have been prepared.

IN reviewing possible routes for the synthesis of dracorubin-type compounds we were attracted by the idea of employing a residue of type (I), containing the flavan system already formed, rather than to attempt the construction of this unit on to a flavylium compound, more especially because of the experimental limitations encountered in the synthesis of the flavan system (Part III, *J.*, 1950, 3117). As a preliminary to exploring this route to the dracorubin system the general procedure developed in Part III (*loc. cit.*) has been extended to the synthesis of a series of flavans from resorcinol, orcinol, quinol, hydroxyquinol, phloroglucinol, and pyrogallol. Further, from some of the formyl- and keto-derivatives it has been possible to obtain, *e.g.*, α- and γ-pyronoflavans, types (II), (III), and (IV).



(I) (II) (III) (IV)

In these studies there emerged several experimental features of general interest which may be noted. (*a*) Most parent flavans are extremely difficult to crystallise and several of the hydroxy-compounds are readily susceptible to aerial oxidation. (*b*) The flavan oxygen system is sensitive to acidic reagents above room temperature and attempts to demethylate *O*-methylflavans by the standard methods are uniformly unsuccessful. Further, whilst, *e.g.*, 8-formyl-7-hydroxyflavan (I; R = CHO) readily reacted with acetophenone in ethereal hydrogen chloride, the resulting flavylium salt was resinous and could not be purified. (*c*) With chromic anhydride *O*-methylflavans furnish low yields of the corresponding flavanones, thus providing a method of detecting the flavan system.

EXPERIMENTAL

7-Hydroxyflavan (I; R = H).—A solution of 7-hydroxyflavanone (Ellison, *J.*, 1927, 1722) (1 g.) in acetic acid (40 ml.), containing concentrated hydrochloric acid (5 ml.), was reduced with zinc amalgam (from 10 g. of zinc dust) at room temperature and 24 hr. later the solution was decanted and diluted with water. Purification of the resulting precipitate from light petroleum (b. p. 60—80°), containing a small amount of methanol, yielded *7-hydroxyflavan* (0·7 g.) in prisms, m. p. 71°, readily soluble in 2N-aqueous sodium hydroxide and having a negative ferric reaction (Found: C, 79·6; H, 6·3. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%).

7-Hydroxy-8-methylflavan (I; R = Me).—(*a*) Prepared by Gattermann's method from 7-hydroxyflavan (1 g.), hydrogen cyanide (5 ml.), and zinc chloride (0·5 g.) in ethereal hydrogen

* Part IV, *J.*, 1952, 4957.

chloride (100 ml.), 8-*formyl*-7-*hydroxyflavan* (*ca.* 0·5 g.) separated from benzene and then methanol in rectangular plates, m. p. 111°, readily soluble in the usual organic solvents, except light petroleum (b. p. 60—80°), and having an intense red-brown ferric reaction in alcohol (Found: C, 75·4; H, 5·9. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·6%); the 2 : 4-*dinitrophenylhydrazone* formed deep red prisms, m. p. 300° (decomp.), from a large volume of ethyl acetate (Found: N, 12·6. $C_{22}H_{18}O_6N_4$ requires N, 12·9%). Reduction of this aldehyde (1 g.) during 24 hr. by the modified Clemmensen technique furnished a good yield of 7-*hydroxy*-8-*methylflavan* which separated from light petroleum (b. p. 60—80°) in prisms (yield, 75%), m. p. 130°, having a negative ferric reaction in alcohol (Found: C, 79·7; H, 6·8. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%).

(*b*) A solution of 3-methylresacetophenone (10 g.), benzaldehyde (10 g.), and potassium hydroxide (20 g.) in a mixture of methanol (50 ml.) and water (20 ml.) was heated under reflux for 4 hr. After dilution with water followed by removal of the excess of benzaldehyde with ether, acidification with concentrated hydrochloric acid gave a yellow viscous liquid which on trituration with ether deposited crude flavanone (3 g.); a further quantity (1·5 g.) was obtained from an acetic acid solution of the residue left on evaporation of the ethereal mother-liquor. 7-*Hydroxy*-8-*methylflavanone* formed prisms, m. p. 219°, from alcohol, moderately soluble in alcohol, acetic acid, and acetone, and sparingly soluble in ether, benzene, and light petroleum (b. p. 60—80°) (Found: C, 75·6; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·6%). Reduction of this flavanone by the modified Clemmensen technique furnished 7-hydroxy-8-methylflavan (yield, *ca.* 80%), m. p. and mixed m. p. 130°.

α-*Pyrono*(6′ : 5′-7 : 8)*flavan* (II; R = H).—The condensation of 8-formyl-7-hydroxyflavan (0·5 g.) and ethyl malonate (0·5 g.) with piperidine (5 drops) at 0° during 24 hr. gave 3′-*ethoxycarbonyl*-α-*pyrono*(6′ : 5′-7 : 8)*flavan* (II; R = CO_2Et) which separated from alcohol in plates (0·5 g.), m. p. 120° (Found: C, 72·0; H, 5·4. $C_{21}H_{18}O_5$ requires C, 72·0; H, 5·2%). An alcoholic solution of this coumarin exhibits a blue fluorescence. Simultaneous hydrolysis and decarboxylation of this coumarin (2 g.) with 20% alcoholic potassium hydroxide (40 ml.) on the steam-bath for 2 hr. furnished α-*pyrono*(6′ : 5′-7 : 8)*flavan* which separated from ethyl acetate–light petroleum (b. p. 60—80°) and then methanol in prisms (1·5 g.), m. p. 153°, insoluble in cold 2N-sodium hydrogen carbonate and -sodium hydroxide (Found: C, 72·7; H, 5·4; H_2O, 6·4. $C_{18}H_{14}O_3,H_2O$ requires C, 73·0; H, 5·4; H_2O, 6·1%).

3′-*Acetyl*-α-*pyrono*-(6′ : 5′-7 : 8)*flavan* (II; R = Ac).—Prepared by the condensation of 8-formyl-7-hydroxyflavan (1 g.) and ethyl acetoacetate (0·8 g.) with piperidine (5 drops) during 24 hr., 3′-*acetyl*-α-*pyrono*(6′ : 5′-7 : 8)*flavan* separated from light petroleum (b. p. 60—80°) or methanol in needles or plates (1·2 g.), m. p. 180° (Found: C, 75·3; H, 5·4. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0%).

Furano(2′ : 3′-7 : 8)*flavan*.—The interaction of 8-formyl-7-hydroxyflavan (1·25 g.), ethyl bromoacetate (0·9 g.), and potassium carbonate (10 g.) in boiling acetone (50 ml.) gave 7-*ethoxycarbonylmethoxy*-8-*formylflavan*, forming needles (1 g.), m. p. 119°, from alcohol (Found: C, 70·4; H, 5·8. $C_{20}H_{20}O_5$ requires C, 70·6; H, 5·9%); the 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate in orange prisms, m. p. 202° (Found: N, 10·9. $C_{26}H_{24}O_8N_4$ requires 10·8%). Simultaneous cyclisation, hydrolysis, and decarboxylation of this ester (1 g.) with boiling 10% alcoholic potassium hydroxide (20 ml.) for 30 min. gave *furano*(2′ : 3′-7 : 8)*flavan* which crystallised from light petroleum and sublimed at 190°/0·01 mm., forming needles (50 mg.), m. p. 182° (Found: C, 81·4; H, 5·5. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%).

7-*Hydroxyflavan*-8-*carboxylic Acid* (I; R = CO_2H) *and its Derivatives*.—Prepared by the pyridine method, 7-*acetoxy*-8-*formylflavan* separated from methanol or ethyl acetate in needles, m. p. 104°, with a negative ferric reaction (Found: C, 72·8; H, 5·5. $C_{18}H_{16}O_4$ requires C, 73·0; H, 5·4%); the 2 : 4-*dinitrophenylhydrazone* formed scarlet needles, m. p. 223°, from ethyl acetate (Found: C, 60·5; H, 4·4; N, 11·8. $C_{24}H_{20}O_7N_4$ requires C, 60·5; H, 4·2; N, 11·8%). This acetoxy-aldehyde (2 g.), in acetone (20 ml.), was oxidised with potassium permanganate (3 g.) in water (80 ml.) added during 1 hr. Next day the mixture was clarified with sulphur dioxide, the acetone evaporated, and the solid crystallised from methanol, giving 7-*acetoxyflavan*-8-*carboxylic acid* in prisms (1·4 g.), m. p. 183°, with a negative ferric reaction (Found: C, 69·3; H, 5·4. $C_{18}H_{16}O_5$ requires C, 69·2; H, 5·2%). Deacetylation of this product (1·4 g.) with warm 2N-aqueous sodium hydroxide (20 ml.) gave a quantitative yield of 7-*hydroxyflavan*-8-*carboxylic acid*, forming plates, m. p. 190°, from methanol, with an intense brownish-blue ferric reaction (Found: C, 71·1; H, 5·5. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%). Prepared with ethereal diazomethane, the *methyl ester* separated from methanol in plates, m. p. 148°, with an

intense brown ferric reaction (Found: C, 71·9; H, 5·8. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·7%). Methylated by the methyl iodide–potassium carbonate method, this ester gave a quantitative yield of *7-methoxy-8-methoxycarbonylflavan*, forming plates, m. p. 107°, from methanol, with a negative ferric reaction [Found: C, 72·6; H, 6·0; OMe, 21·0. $C_{16}H_{12}O_2(OMe)_2$ requires C, 72·5; H, 6·1; OMe, 20·8%].

6-Formyl-7-hydroxy-8-methylflavan.—Prepared from 7-hydroxy-8-methylflavan (1 g.) by Gattermann's method, this *flavan* separated from methanol in prisms (0·5 g.), m. p. 121°, with an intense violet-brown ferric reaction (Found: C, 75·9; H, 6·4. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%); the 2 : 4-*dinitrophenylhydrazone* formed scarlet plates, m. p. 277°, from ethyl acetate (Found: N, 12·5. $C_{23}H_{20}O_6N_4$ requires N, 12·5%). By the ethyl malonate–piperidine method this aldehyde (0·5 g.) furnished *3'-ethoxycarbonyl-8-methyl-α-pyrono(5' : 6'-6 : 7)flavan* (IV; R = CO_2Et), forming plates (0·6 g.), m. p. 174°, from light petroleum (b. p. 60—80°) (Found: C, 72·5; H, 5·3. $C_{22}H_{20}O_5$ requires C, 72·5; H, 5·5%). An alcoholic solution of this has a violet fluorescence.

Hydrolysis of the ethoxycarbonylcoumarin (1 g.) with boiling 10% alcoholic potassium hydroxide (20 ml.) for 1 hr. gave *8-methyl-α-pyrono(5' : 6'-6 : 7)flavan* (IV; R = H) in plates (0·5 g.), m. p. 167°, from light petroleum (b. p. 80—100°) or methanol, insoluble in cold 2N-sodium hydroxide (Found: C, 73·0; H, 5·5. $C_{19}H_{16}O_3,H_2O$ requires C, 73·5; H, 5·9%).

8-Acetyl-7-hydroxyflavan (I; R = Ac).—Prepared from 7-hydroxyflavan in moderate yield by the Hoesch method, *8-acetyl-7-hydroxyflavan* formed prisms, m. p. 143°, from methanol, with an intense brown ferric reaction (Found: C, 75·8; H, 5·8. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%); the 2 : 4-*dinitrophenylhydrazone* separated from much ethyl acetate in red plates, m. p. 242° (Found: N, 12·2. $C_{23}H_{20}O_6N_4$ requires N, 12·5%). This flavan (1·5 g.) was heated on the steam-bath with ethyl acetate (10 ml.) and powdered sodium (1·4 g.) for 1 hr. and on isolation the resulting mixed diketone and chromone were boiled with alcohol (10 ml.), containing concentrated hydrochloric acid (6 drops), for 10 min., giving *2'-methyl-γ-pyrono(6' : 5'-7 : 8)-flavan* which separated from light petroleum (b. p. 80—100°) and then from methanol in prisms (0·5 g.), m. p. 158°, insoluble in 2N-sodium hydroxide and having a negative ferric reaction (Found: C, 78·3; H, 5·8. $C_{19}H_{16}O_3$ requires C, 78·1; H, 5·5%).

8-Ethyl-7-hydroxyflavanone.—Prepared from 3-ethyl resacetophenone (Limaye and Limaye, *Rasayanam*, 1937, **1**, 109; *Chem. Abs.*, 1938, **32**, 2095) (5 g.) and benzaldehyde (5 g.), in the usual manner, *8-ethyl-7-hydroxyflavanone* formed prisms (2 g.), m. p. 294°, from ethyl acetate (Found: C, 75·9; H, 6·1. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%).

6-Ethyl-7-hydroxyflavan.—Prepared from 5-ethylresacetophenone (Weiss and Kratz, *Monatsh.*, 1929, **51**, 386) (10 g.) and benzaldehyde (10 g.), *6-ethyl-7-hydroxyflavanone* separated in plates (6·2 g.), m. p. 243°, from methanol (Found: C, 76·0; H, 6·0%). Reduction of this gave a high yield of *6-ethyl-7-hydroxyflavan*, forming prisms, m. p. 118°, from aqueous methanol (Found: C, 80·3; H, 7·3. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

7-Hydroxy-6-methylflavan.—From 5-methylresacetophenone (Yanagita, *Ber.*, 1938, **71**, 2270) (11 g.) and benzaldehyde (10 g.), *7-hydroxy-6-methylflavanone* separated from acetic acid in plates (6·2 g.), m. p. 234—236° (Found: C, 75·8; H, 5·7. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·6%). Reduction of this gave *7-hydroxy-6-methylflavan*, in prisms, m. p. 119°, from methanol (Found: C, 75·9; H, 6·5. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%); mixed with isomeric 7-hydroxy-8-methylflavan, this had m. p. *ca.* 80°. Application of the Gattermann aldehyde synthesis to this flavan (1·0 g.) furnished *8-formyl-7-hydroxy-6-methylflavan*, yellow needles (0·4 g.), m. p. 120° (from methanol), with an olive-green ferric reaction in alcohol (Found: C, 76·0; H, 5·6. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%); the 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate in orange needles, m. p. 265° (Found: N, 12·2. $C_{23}H_{20}O_6N_4$ requires N, 12·5%). Prepared from this aldehyde (0·3 g.) and ethyl malonate in the usual way, *3'-ethoxycarbonyl-6-methyl-α-pyrono(6' : 5'-7 : 8)flavan* separated from alcohol in yellow needles (0·25 g.), m. p. 160° (Found: C, 72·4; H, 5·7. $C_{22}H_{20}O_5$ requires C, 72·5; H, 5·5%).

7-Methoxyflavan.—Reduction of 7-methoxyflavanone (Kostanecki and Stoppani, *Ber.*, 1904, **37**, 1180) (5 g.) furnished *7-methoxyflavan* as a colourless liquid (3·5 g.), b. p. 130°/0·001 mm. (Found: C, 80·4; H, 6·7. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%). Demethylation of this compound with aluminium chloride or hydriodic acid, under a variety of conditions, yielded only intractable products.

Oxidation of 7-methoxyflavan (0·5 g.), dissolved in acetic acid (30 ml.) [by the addition of a solution of chromic oxide (0·5 g.) in acetic acid (10 ml.)], on the steam-bath during 30 min. furnished a viscous oil from which warm light petroleum (b. p. 80—100°) extracted 7-methoxyflavanone (50 mg.), identical with an authentic specimen (*loc. cit.*).

5-Hydroxyflavan.—The reduction of 5-hydroxyflavanone (1 g.) (Narasimhachari and Seshadri, *Proc. Indian Acid. Sci.*, 1948, **27**, *A*, 223) by the usual method gave *5-hydroxyflavan*, plates (0·8 g.), m. p. 160°, from light petroleum (b. p. 80—100°) containing a trace of methanol (Found: C, 79·6; H, 6·0. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%). Similarly, 5-methoxyflavanone (*idem, ibid.*) (1·0 g.) yielded *5-methoxyflavan*, plates (0·75 g.), m. p. 60°, from ethanol (Found: C, 79·8; H, 6·8. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%). Oxidation of this flavan (0·5 g.) with chromic oxide (as for the 7-methoxy-analogue) regenerated 5-methoxyflavanone (50 mg.).

7-Hydroxy-5-methylflavan.—A mixture of orcacetophenone (10 g.), benzaldehyde (7·5 g.), methanol (60 ml.), water (20 ml.), and potassium hydroxide (20 g.) was boiled during 3½ hr., diluted with water, extracted with ether, and acidified with hydrochloric acid. The solid (14 g.) was triturated with cold benzene and then crystallised from ethyl acetate, giving *7-hydroxy-5-methylflavanone* in plates (11·5 g.), m. p. 212° (Found: C, 75·4; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·6%). Reduction of this furnished 7-hydroxy-5-methylflavan, needles, m. p. 82—85° (from methanol), which in moist air readily oxidised to a sticky resin and so was utilised immediately for the subsequent operations.

Prepared from this flavan by Gattermann's method, *8-formyl-7-hydroxy-5-methylflavan* separated from light petroleum (b. p. 80—100°) or methanol in prisms, m. p. 127°, with an intense red-brown ferric reaction in alcohol (yield, 50%) (Found: C, 76·0; H, 6·0. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%); the 2 : 4-*dinitrophenylhydrazone* formed scarlet needles, m. p. 276—278° (decomp.), from ethyl acetate (Found: N, 12·5. $C_{23}H_{20}O_6N_4$ requires N, 12·5%). Reduction of the aldehyde (1 g.) gave *7-hydroxy-5 : 8-dimethylflavan* in needles (0·7 g.), m. p. 117°, from light petroleum (b. p. 60—80°) which became brown during 24 hr. (Found: C, 80·4; H, 7·1. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%). Prepared from this aldehyde (1 g.) and ethyl malonate (0·7 g.) in the usual manner, *3′-ethoxycarbonyl-5-methyl-α-pyrono*(6′ : 5′-7 : 8)*flavan* separated from light petroleum (b. p. 80—100°) in plates (1·2 g.), m. p. 144° (Found: C, 72·8; H, 5·8. $C_{22}H_{20}O_5$ requires C, 72·5; H, 5·5%). Similarly, the aldehyde (0·5 g.) and ethyl acetoacetate (0·3 g.) furnished *3′-acetyl-5-methyl-α-pyrono*(6′ : 5′-7 : 8)*flavan*, pale yellow plates (0·7 g.), m. p. 103° [from light petroleum (b. p. 80—100°)] (Found: C, 75·1; H, 5·1. $C_{21}H_{18}O_4$ requires C, 75·4; H, 5·4%).

Derivatives of 5-Hydroxy-7-methoxyflavan.—Prepared by the interaction of 5-hydroxy-7-methoxyflavan (Part III, *loc. cit.*) (1 g.), hydrogen cyanide (5 ml.), and zinc chloride (0·5 g.), in ethereal hydrogen chloride, the semi-solid aldimine complex was hydrolysed with warm water, and the product repeatedly extracted with light petroleum (b. p. 80—100°). Crystallised from methanol, the residue gave *6-formyl-5-hydroxy-7-methoxyflavan* in pale yellow needles (0·15 g.), m. p. 99°, with an intense red-brown ferric reaction (Found: C, 71·6; H, 5·8; OMe, 10·6. $C_{16}H_{13}O_3$·OMe requires C, 71·8; H, 5·7; OMe, 10·9%). The light petroleum extract contained *8-formyl-5-hydroxy-7-methoxyflavan*, forming plates (0·4 g.), m. p. 211°, from methanol, with a negative ferric reaction (Found: C, 71·6; H, 5·8; OMe, 10·9. $C_{16}H_{13}O_3$·OMe requires C, 71·8; H, 5·7; OMe, 10·9%). The 2 : 4-*dinitrophenylhydrazone* separated from ethanol in red plates, m. p. 214° (Found: N, 11·8. $C_{23}H_{20}O_7N_4$ requires N, 12·1%).

Obtained from 5-hydroxy-7-methoxyflavan (1 g.), by the Hoesch method, *8-acetyl-5-hydroxy-7-methoxyflavan* separated from methanol in prisms (0·4 g.), m. p. 152°, with a negative ferric reaction (Found: C, 72·3; H, 6·3. $C_{18}H_{18}O_4$ requires C, 72·5; H, 6·1%). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol in red prisms, m. p. 154° (decomp.) (Found: N, 12·0. $C_{24}H_{22}O_7N_4$ requires N, 11·7%).

8-Formyl-7-hydroxy-5-methoxyflavan.—The reduction of 7-benzyloxy-5-hydroxyflavanone (Part III, *loc. cit.*) (1 g.) furnished *7-benzyloxy-5-hydroxyflavan*, prisms (0·7 g.), m. p. 139°, from methanol (Found: C, 79·4; H, 6·1. $C_{22}H_{20}O_3$ requires C, 79·5; H, 6·1%).

Similarly, 7-benzyloxy-5-methoxyflavanone (Part III, *loc. cit.*) gave *7-benzyloxy-5-methoxyflavan*, prisms, m. p. 71° (from ether) (Found: C, 80·1; H, 6·3. $C_{23}H_{22}O_3$ requires C, 79·7; H, 6·4%). By the Gattermann aldehyde synthesis this flavan (1 g.) yielded *7-benzyloxy-8-formyl-5-methoxyflavan* (0·6 g.), plates, m. p. 200° (from methanol), with a negative ferric reaction (Found: C, 76·9; H, 5·9. $C_{24}H_{22}O_4$ requires C, 77·0; H, 5·9%); the 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate in red prisms, m. p. 249—250° (Found: N, 10·2. $C_{30}H_{26}O_7N_4$ requires N, 10·1%). Debenzylation of this compound with hydrogen and a palladium–charcoal catalyst furnished 8-formyl-7-hydroxy-5-methoxyflavan, m. p. and mixed m. p. 128° (Part III, *loc. cit.*).

Prepared from 8-formyl-7-hydroxy-5-methoxyflavan (1 g.) and ethyl malonate (0·7 g.) with piperidine (5 drops), *3′-ethoxycarbonyl-5-methoxy-α-pyrono*(6′ : 5′-7 : 8)*flavan* separated from

alcohol in colourless plates (1·1 g.), m. p. 192°, an alcoholic solution of which exhibits a violet fluorescence (Found: C, 69·1; H, 5·1. $C_{22}H_{30}O_6$ requires C, 69·5; H, 5·3%). Hydrolysis and simultaneous decarboxylation of this ester (1 g.) with boiling 10% alcoholic potassium hydroxide (20 ml.) for 1 hr. gave *5-methoxy-α-pyrono(6′ : 5′-7 : 8)flavan*, plates (0·8 g.), m. p. 263°, from dioxan, insoluble in cold 2N-aqueous sodium hydroxide (Found: C, 69·6; H, 5·7; H_2O, 5·6. $C_{19}H_{16}O_4,H_2O$ requires C, 69·9; H, 5·6; H_2O, 5·5%).

Condensation of 8-formyl-7-hydroxy-5-methoxyflavan (0·5 g.) and ethyl acetoacetate (0·35 g.) by the piperidine method furnished *3′-acetyl-5-methoxy-α-pyrono(6′ : 5′-7 : 8)flavan*, yellow prisms (0·5 g.), m. p. 210° (from alcohol) (Found: C, 72·4; H, 4·8; OMe, 8·9. $C_{20}H_{18}O_4$·OMe requires C, 72·0; H, 5·2; OMe, 8·9%).

6-Formyl-7-hydroxy-5-methoxy-8-methylflavan.—Prepared from 7-hydroxy-5-methoxy-8-methylflavan (Part III, *loc. cit.*) (1 g.) by the Gattermann method, the *aldehyde* separated from methanol in prisms (0·3 g.), m. p. 146°, with an intense red-brown ferric reaction (Found: C, 72·4; H, 6·2; OMe, 10·3. $C_{17}H_{15}O_3$·OMe requires C, 72·5; H, 6·1; OMe, 10·4%); the *2 : 4-dinitrophenylhydrazone* crystallised from ethyl acetate–ethanol in deep red prisms, m. p. 239° (Found: N, 11·5. $C_{24}H_{22}O_7N_4$ requires N, 11·7%). By the standard methods this aldehyde (0·5 g.) gave *3′-ethoxycarbonyl-5-methoxy-8-methyl-α-pyrono(5′ : 6′-6 : 7)flavan*, forming plates (0·45 g.), m. p. 144°, from methanol (Found: C, 70·4; H, 5·7. $C_{23}H_{22}O_6$ requires C, 70·0; H, 5·6%), and 7-hydroxy-5-methoxyflavan (1 g.) gave *8-acetyl-7-hydroxy-5-methoxyflavan* (0·5 g.), prisms, m. p. 148° (from alcohol), with an intense violet-brown ferric reaction (Found: C, 72·2; H, 6·2. $C_{18}H_{18}O_4$ requires C, 72·5; H, 6·1%). Heated with ethyl acetate (10 ml.) and sodium (1·5 g.) on the steam-bath for 1 hr., this ketone (1·5 g.) furnished *5-methoxy-2′-methyl-γ-pyrono-(6′ : 5′-7 : 8)flavan*, yellow prisms (1·5 g.), m. p. 215°, from light petroleum (b. p. 80—100°) (Found: C, 74·1; H, 5·9. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6%), which on condensation with piperonaldehyde under standard conditions gave *5-methoxy-3″ : 4″-methylenedioxystyryl-γ-pyrono(6′ : 5′-7 : 8)flavan*, forming orange prisms, m. p. 222°, from light petroleum (b. p. 80—100°) (Found: C, 74·3; H, 5·0. $C_{28}H_{22}O_6$ requires C, 74·0; H, 4·9%).

Boiled for 3½ hr., a mixture of 8-acetyl-7-hydroxy-5-methoxyflavan (1·5 g.), benzaldehyde (0·75 g.), potassium hydroxide (4 g.), methanol (10 ml.), and water gave *8-cinnamoyl-7-hydroxy-5-methoxyflavan* which separated from light petroleum (b. p. 80—100°) in yellow prisms (1 g.), m. p. 204°, with an intense red-brown ferric reaction (Found: C, 77·6; H, 5·6; OMe, 8·0. $C_{24}H_{21}O_3$·OMe requires C, 77·3; H, 6·2; OMe, 8·0%).

5 : 7-Dimethoxyflavan.—Obtained from 5 : 7-dimethoxyflavanone (Shinoda and Sato, *J. Pharm. Soc., Japan*, 1928, **48**, 111), *5 : 7-dimethoxyflavan* separated from methanol in prisms, m. p. 137° (Found: C, 75·2; H, 6·8. $C_{17}H_{18}O_3$ requires C, 75·5; H, 6·7%). On being heated under reflux for 1 hr. with aluminium chloride (2 g.) and benzene (20 ml.), the flavan (1 g.) gave 5-hydroxy-7-methoxyflavan (0·6 g.), m. p. and mixed m. p. 204°. Attempts to demethylate the dimethoxyflavan with hot hydriodic acid were unsuccessful.

Oxidation of 5 : 7-dimethoxyflavan with chromic oxide furnished a low yield of 5 : 7-dimethoxyflavanone, m. p. and mixed m. p. 144—145°.

6-Hydroxyflavan.—*6-Hydroxyflavanone* [from 2 : 5-dihydroxyacetophenone (10 g.) and benzaldehyde (7·5 g.)] separated from methanol in prisms (7·2 g.), m. p. 220° (Found: C, 75·4; H, 5·3. $C_{15}H_{12}O_3$ requires C, 75·0; H, 5·0%), and on reduction by the standard method gave *6-hydroxyflavan*, forming prisms (75%), m. p. 119°, from methanol (Found: C, 79·9; H, 6·1. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2). By the Gattermann method this gave a low yield of *8-formyl-6-hydroxyflavan*, plates, m. p. 102° (from methanol), with a negative ferric reaction (Found: C, 75·7; H, 5·7. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·6%).

6-Hydroxy-7-methoxyflavan.—Condensation of 2 : 5-dihydroxy-4-methoxyacetophenone (10 g.) with benzaldehyde (5 ml.) in the usual manner gave a mixture which on fractional crystallisation from alcohol furnished the sparingly soluble *chalkone* in orange needles (*ca.* 2 g.), m. p. 177°, with an intense green-brown ferric reaction (Found: C, 71·3; H, 5·2; OMe, 11·7. $C_{16}H_{11}O_3$·OMe requires C, 71·1; H, 5·2; OMe, 11·5%), and the more easily soluble *flavanone* (6·2 g.) in plates, m. p. 173°, with a negative ferric reaction (Found: C, 71·2; H, 5·4; OMe, 11·6%). This flavanone (1 g.) was readily reduced to *6-hydroxy-7-methoxyflavan*, prisms (0·8 g.), m. p. 112° (from dilute methanol) (Found: C, 74·7; H, 6·5; OMe, 12·1. $C_{15}H_{13}O_2$·OMe requires C, 75·0; H, 6·3; OMe, 12·1%).

7 : 8-Dimethoxyflavan.—By the methyl iodide–potassium carbonate method 7 : 8-dihydroxyflavanone (Geissmann and Clinton, *J. Amer. Chem. Soc.*, 1946, **68**, 697) gave *7 : 8-dimethoxyflavanone*, forming prisms, m. p. 120°, from light petroleum (b. p. 60—80°) [Found: C, 71·5; H, 5·4; OMe, 21·6. $C_{15}H_{10}O_2(OMe)_2$ requires C, 71·8; H, 5·7; OMe, 21·8%], which on reduction

yielded 7 : 8-*dimethoxyflavan*, prisms (*ca.* 70%), m. p. 100° (from methanol) [Found: C, 75·1; H, 6·7; OMe, 23·9. $C_{15}H_{12}O(OMe)_2$ requires C, 75·5; H, 6·7; OMe, 23·0%].

Reduction of 7 : 8-dihydroxyflavanone yielded the flavan as colourless needles, which rapidly darkened and could not be purified.

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Spectrophotometric Titrations involving the Higher Oxidation State of Ferrimyoglobin.

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According to spectrophotometric titrations with ascorbic acid (AH_2), ferromyoglobin ($MbFe^{2+},H_2O$), and oxymyoglobin [$MbFe(II)O_2^{2+}$] as reducing agents, the intermediate compound formed when ferrimyoglobin [$MbFe^{3+},H_2O$] reacts with hydrogen peroxide is one oxidation equivalent above the ferric state of the hæmoprotein, in conformity with the previous result obtained by using potassium ferrocyanide. Hence this higher oxidation state has properties characteristic of a quadrivalent iron compound [MbFe(IV)] and the reactions can be represented: *

$$2MbFe(IV) + AH_2 \longrightarrow 2MbFe^{3+},H_2O + A$$
$$MbFe(IV) + MbFe^{2+},H_2O \longrightarrow 2MbFe^{3+},H_2O$$
$$MbFe(IV) + MbFe(II)O_2^{2+} \longrightarrow 2MbFe^{3+},H_2O + O_2$$

SPECTROPHOTOMETRIC titration of the intermediate compound which is formed when ferrimyoglobin reacts with peroxides, with potassium ferrocyanide as reducing agent, showed that this compound is a single equivalent oxidation product (George and Irvine, *Nature*, 1951, **168**, 164; *Biochem. J.*, 1952, **52**, 511; 1953, **55**, 230). Since in ferrimyoglobin the iron is in the ferric state, the intermediate compound has the oxidation–reduction characteristics of a quadrivalent iron derivative. Its relation to ferrimyoglogin, represented by $MbFe^{3+},H_2O$, can thus be summarised:

$$MbFe^{3+},H_2O \longrightarrow MbFe(IV) + e^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where MbFe(IV) denotes the higher oxidation state.

Recent experiments (George and Irvine, Symp. on Co-ordination Chemistry, Copenhagen, 1953, Danish Chem. Soc., in the press) are in accord with a "ferryl ion" type of structure for MbFe(IV), which, if further substantiated, would require reaction (1) to be amplified as follows:

$$MbFe^{3+},H_2O \longrightarrow MbFe(IV)O^{2+} + 2H^+ + e^-$$

But further confirmation of the single equivalent oxidation is desirable because the stoicheiometry of the oxidation process is the basis of all further work and gives the intermediate compound its particular significance. MbFe(IV) would be the first compound

* The following conventions have been adopted: $MbFe^{2+},H_2O$ and $MbFe^{3+},H_2O$ denote ferro- and ferri-myoglobin respectively in which the superscripts 2+ and 3+ indicate that the iron is ionically bound, and the sixth co-ordination position is occupied by a water molecule. In these and the other compounds the five remaining positions are occupied by four bonds in a plane to pyrrole-nitrogen atoms and one bond to the protein. $MbFe(II)O_2^{2+}$ denotes oxymyoglobin, the symbol (II) indicating a covalently bonded complex of ferrous iron. MbFe(IV) denotes the higher oxidation state which also has covalently bonded iron, but the formula cannot be completed because the structure has not yet been established with certainty. The equations in which MbFe(IV) occurs cannot therefore be balanced, and are only to be taken as a correct representation of the interchange of oxidation equivalents: there is evidence in some cases that hydrogen ions are also involved, and it is through their participation that the ionic charges on reactants and products become equal. This usage is somewhat similar to that current in the U.S.A. where the roman superscripts are occasionally used to denote generalised reactions between various oxidation states.

of its type to be well authenticated, and, from the point of view of its oxidation–reduction behaviour, it appears to be analogous to the second of the two intermediate compounds formed by the hæmoprotein enzymes, peroxidase and catalase, with peroxides. The action of these enzymes has until recently been considered almost exclusively in terms of enzyme–substrate complex formation, *i.e.*, $E + S \rightleftharpoons [ES]$, etc. (see, *e.g.*, Chance, "Modern Trends in Physiology and Biochemistry," Academic Press Inc., New York, 1952, p. 25), but now a new mechanism with two single equivalent reduction steps linking the two intermediate compounds takes its place (George, *Adv. Catalysis*, 1952, **4**, 367; *Biochem. J.*, 1952, **53**, xix; 1953, **54**, 267).

The intermediate compound was formed as in the previous experiments (George and Irvine, *loc. cit.*, 1952) by adding the minimal quantity of hydrogen peroxide to ferrimyoglobin in borate buffer of pH 8·6. At this pH no side reactions occur. At other pH values, where this would not be the case, the intermediate compound was first made in very weak buffer of pH 8·6 and then transferred to a stronger buffer of the required pH. The results of spectrophotometric titrations with ascorbic acid as reducing agent are given in the Table. The titrations at pH 8·6 were carried out in the absence of oxygen to over-

Reduction of the intermediate compound, present in excess, with ascorbic acid at ~18°.

	At pH 5·9 in air					At pH 8·6, O_2 absent		
Concn. (10^{-6}M) of ascorbic acid present initially (*a*)	4·5	9·0	9·0	15·0	15·0	9·0	15·0	15·0
Concn. (10^{-6}M) of intermediate compound present initially	32·0	32·0	32·0	32·0	32·0	26·3	33·8	37·5
Intermediate compound (10^{-6} mole) reduced by ascorbic acid (*b*)	10·7	18·2	17·7	30·1	27·2	17·5	27·9	25·8
Ratio: *a*/*b*	0·42	0·49	0·51	0·50	0·55	0·51	0·54	0·59
		(Mean, 0·49 ± 0·03)				(Mean, 0·55 ± 0·03)		

come the difficulties caused by autoxidation of the ascorbic acid. Not only is ascorbic acid destroyed by autoxidation, but also the hydrogen peroxide so formed oxidises some ferrimyoglobin. At pH 5·9 reduction was much faster than at pH 8·6 so that the effect of autoxidation was negligible, particularly when quartz-distilled water, free from traces of copper, was used. It will be seen from the Table that approximately 0·5 mole of ascorbic acid (AH_2) reduces one mole of the intermediate compound to ferrimyoglobin in an overall reaction showing the following stoicheiometric relation:

$$2MbFe(IV) + AH_2 \longrightarrow 2MbFe^{3+},H_2O + A$$

Experiments were also carried out with ferromyoglobin [$MbFe^{2+},H_2O$] and oxymyoglobin [$MbFe(II)O_2^{2+}$] as reducing agents. Even though the latter contains an oxygen molecule bonded to the iron, oxymyoglobin still reacts as a ferrous complex; for instance, addition of potassium ferricyanide oxidises it to the ferric state (ferrimyoglobin) and the oxygen is liberated as such. In these experiments equimolar quantities (5×10^{-5}M) of the intermediate compound and the reducing agent were mixed, then when reduction was complete sodium azide was added. The spectrum of the azide complex thus obtained was then compared with that of the azide complex made from an equivalent concentration of fresh ferrimyoglobin. With ferromyoglobin the experiments were conducted in the absence of oxygen to eliminate the formation of oxymyoglobin. The results are illustrated in the Figure, which shows that equimolar quantities of the intermediate compound and ferromyoglobin or oxymyoglobin give almost solely two equivalents of ferrimyoglobin. These reactions can thus be written

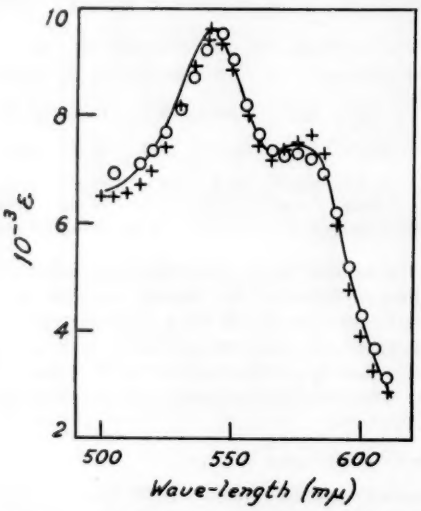
$$MbFe(IV) + MbFe^{2+},H_2O \longrightarrow 2MbFe^{3+},H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$MbFe(IV) + MbFe(II)O_2^{2+} \longrightarrow 2MbFe^{3+},H_2O + O_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Both reactions were relatively slow, requiring 20—30 minutes for completion with 5×10^{-5}M-solutions at pH 8·6. As an approximation, if 97% reaction occurred in 20 minutes, the bimolecular velocity constant would be about 500 l. mole^{-1} sec.$^{-1}$. In more acid solutions the reactions were faster. The slow rate must be attributed either to the way in which the intermediate compound acts as an oxidising agent or to the fact that

reaction is between two hæmoprotein molecules, for both ferromyoglobin and oxymyoglobin react with electron-transfer oxidising agents, *e.g.*, potassium chloroiridate, with velocity constants greater than 10^5 l. mole^{-1} sec.$^{-1}$ (George and Irvine, *J.*, 1954, 587). The first is the more likely explanation since the comparable reaction of ferrocytochrome-*c* with the higher oxidation state of cytochrome-*c* peroxidase (two other hæmoproteins) is much faster, reaching completion in less than 15 seconds with about 10^{-6}M-solutions (George, *Biochem. J.*, 1953, **54**, 267). A lower limit of about 3×10^6 l. mole^{-1} sec.$^{-1}$ is obtained for the velocity constant on the assumption that 97% reaction occurs in 10 seconds.

These titrations thus confirm the view that ferrimyoglobin undergoes single equivalent oxidation when it reacts with peroxide. The participation of higher oxides of iron, Fe_2O_4 and Fe_2O_5, as intermediates in the reactions of iron salts with peroxide, was often proposed before free-radical mechanisms were advanced (see, *e.g.*, Hale, *J. Phys. Chem.*, 1929, **33**, 1633), and later Polonovski, Jayle, and Glotz (*Bull. Soc. Chim. biol.*, 1939, **21**, 48) suggested the formation of a quadrivalent iron intermediate in the ferrihæmoglobin–peroxide reaction. Polonovski, Jayle, and Fraudet (*Compt. rend.*, 1941, **213**, 740)



Absorption spectra of the azide complex formed from the products of the reduction of the intermediate compound with an equimolecular concentration of ferromyoglobin (○) *and oxymyoglobin* (+), *and that formed from an equivalent concentration of fresh ferrimyoglobin* (*smooth curve*).

attempted to confirm its formation by potentiometric titration; but we have shown (George and Irvine, *Biochem. J.*, 1954, **58**, 188) that this evidence for the formation of the higher oxidation state is not unequivocal.

The reduction of the intermediate compound with ferromyoglobin and oxymyoglobin (reactions 2 and 3), together with the similar reaction of ferrocytochrome-*c* cited above, provide examples of disproportionation between various oxidation states of a transition element which are very familiar for some transition elements but have hitherto not been demonstrated for iron: reactions between ferrous or ferric salts and the ferrates [Fe(VI) in FeO_4^{2-}] cannot be studied because the former are soluble only in acid solution and the latter stable only in alkaline solution, decomposing with the liberation of oxygen if the solution is acidified.

Experimental

Ferrimyoglobin, Oxymyoglobin, and Ferromyoglobin.—The preparation of ferrimyoglobin has been described (George and Irvine, *loc. cit.*, 1952). The oxygen complex of ferromyoglobin was obtained by reducing a solution of ferrimyoglobin at the required pH with sodium dithionite (hydrosulphite) in slight excess, then shaking the solution in air until all the dithionite was oxidised. The formation of oxymyoglobin was indicated by the change from brown to pink, and identified by the characteristic absorption bands at 542 and 580 mμ. Ferromyoglobin was prepared by deoxygenating oxymyoglobin in the apparatus described below.

Ascorbic Acid.—Analytical-grade L-ascorbic acid was dissolved in quartz-distilled water immediately before use, in flasks which had been thoroughly flushed with nitrogen.

Buffer Solutions.—The buffer solution of pH 8·6 was prepared from 0·3M-solutions of boric acid and sodium hydroxide according to the procedure of Clark and Lubs. The phosphate buffer of pH 5·9 was made from 0·04M-solutions of sodium dihydrogen phosphate and sodium hydroxide.

Experiments in the Absence of Oxygen.—The apparatus was a boat-shaped vessel of about 10 ml. capacity, having a side-arm with a ground-glass joint into which a tube containing the second reactant could be fitted. The vessel had also two outlets which could be closed by taps, one of which was attached to a high-vacuum pump. There was a lead from the apparatus to a source of oxygen-free nitrogen, obtained by passing the highest grade of cylinder nitrogen over copper at 400°.

One solution was placed in the vessel and the other in the tube attached to the side-arm; both solutions were evacuated with constant shaking, and the apparatus was then flushed with nitrogen. This process was repeated 2—3 times and after a final evacuation the solutions were mixed and allowed to react *in vacuo*. To minimise losses due to evaporation the vessel was immersed in ice–salt during evacuation.

In the experiments with ferromyoglobin, oxymyoglobin was placed in the side-arm, and deoxygenation and reduction were carried out in the same apparatus.

Spectrophotometric Measurements.—Measurements were made with a Unicam Quartz Spectrophotometer. In the reduction experiments with ascorbic acid the measurements of optical density were made at 549 mμ, with 1 cm. cuvettes. From the optical density of a ferrimyoglobin solution of a specified concentration and the maximum change produced on addition of hydrogen peroxide, which can be taken to correspond to complete conversion into the intermediate compound, the concentration of intermediate compound reacting with added ascorbic acid was calculated.

For reductions with ferromyoglobin and oxymyoglobin, the extinction coefficients of the azide complex shown in the Figure were obtained by assuming that the reduction product was entirely ferrimyoglobin.

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Mechanism of the Kolbe–Schmitt Reaction. Part I. Infra-red Studies.

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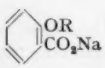
Examination of the infra-red absorption spectrum of the product obtained by carboxylation of sodium phenoxide (Kolbe–Schmitt reaction) shows that the sodium is attached to the carboxyl group, thus disproving Tijmstra's suggestion (*Ber.*, 1905, **38**, 1375) that the product has the metal oxide structure. Various reaction mechanisms are examined and some evidence is presented in support of the theory of cation-induced electrophilic replacement in the aromatic nucleus.

VARIOUS theories have been advanced to explain the mechanism of the carboxylation of alkali-metal aryloxides by carbon dioxide under pressure (Kolbe–Schmitt reaction). These postulate, respectively, initial formation of a metal aryl carbonate which subsequently rearranges (Schmitt, *J. pr. Chem.*, 1885, **31**, 397), direct carboxylation of the aromatic nucleus (Lobry de Bruyn and Tijmstra, *Rec. Trav. chim.*, 1904, **23**, 385; Tijmstra, *Ber.*, 1905, **38**, 1375; Schwenk *et al.*, *Chem. Ztg.*, 1929, **53**, 297, 333; Silin and Moschinskaya, *J. Gen. Chem., U.S.S.R.*, 1938, **8**, 810), alkali-metal-induced electrophilic replacement of nuclear hydrogen by carboxyl with migration of the alkali metal to the carboxyl group (Johnson, *J. Amer. Chem. Soc.*, 1933, **55**, 3029; Seel, *Angew. Chem.*, 1948, **60**, 300; cf. Henecka, "Chemieder β-Dicarbonylverbindungen," Springer-Verlag, Berlin, 1950, p. 164), and carboxylation of an *ortho*-metallated intermediate (Gilman, Arntzen, and

Webb, *J. Org. Chem.*, 1945, **10**, 374). The mechanism suggested by Gershzon (*J. Gen. Chem., U.S.S.R.*, 1943, **13**, 68) was later disproved (*ibid.*, 1946, **16**, 1485). A useful summary of current knowledge of the Kolbe–Schmitt reaction has been given by Wessely *et al.* (*Monatsh.*, 1950, **81**, 1071).

In the case of sodium phenoxide, direct substitution of carbon dioxide in the activated aromatic nucleus with retention of the metal-oxide structure (I; R = H) was postulated by Tijmstra (*loc. cit.*) whereas, according to the other views of the reaction, the product is a metal carboxylate (II; R = H). By a study of the infra-red absorption spectra we have sought to distinguish between these alternative structures. The preliminary results have already been reported (Hales, Jones, and Lindsey, *Chem. and Ind.*, 1954, 49).

(I)  (II)

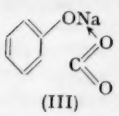
It is known that the asymmetric stretching of the ionised carboxyl group, ν_a (C···O), gives rise to a strong absorption band near 1600 cm.$^{-1}$ (see, *e.g.*, Thomas, *Discuss. Faraday Soc.*, 1950, **9**, 339). This is so for potassium phenylacetate (Davies and Thomas, *J.*, 1951, 2858) and we find likewise that sodium benzoate (1600 cm.$^{-1}$), sodium salicylate (1600 cm.$^{-1}$), and sodium *o*-methoxybenzoate (1613 cm.$^{-1}$) all give rise to strong bands in this region. Flett (*J.*, 1951, 962) has demonstrated that carboxylic acids give rise in general to five recognisable absorption bands, the first, due to associated OH, in the region 2700—2500, the others at ~1700, 1420, 1250, and 900 cm.$^{-1}$, the 1700 and 1250 cm.$^{-1}$ bands being the strongest. We have confirmed his results in the case of benzoic and salicylic acid; the spectrum of *o*-methoxybenzoic acid, which shows bands at 2605, 1689, 1669, 1412, 1258, and 921 cm.$^{-1}$, lends additional support. The doublet (1689, 1669 cm.$^{-1}$) here may possibly be due to a splitting of the single frequency owing to symmetry of the crystal lattice; alternatively two possible molecular configurations might exist in the solid state corresponding to the free and internally hydrogen-bonded hydroxyl groups (Davies, *Chem. and Ind.*, 1953, 614). Although Flett's work indicates that the strong 1258-cm.$^{-1}$ band of *o*-methoxybenzoic acid arises from the carboxyl group, the position of the band falls well outside the limits of 1300 $\pm$ 15 cm.$^{-1}$ suggested by Hadzi and Sheppard (*Proc. Roy. Soc.*, 1953, *A*, **216**, 247), and comparison with benzoic acid might suggest that the medium 1289-cm.$^{-1}$ band arises from the carboxyl group. In the case of potassium hydrogen phthalate, bands indicating the presence of both ionised and non-ionised carboxyl groups are present, the relevant bands being 1603 (ionised) and 1669 cm.$^{-1}$ (non-ionised) (cf. Davison, *Chem. and Ind.*, 1953, 408; Cardwell, Dunitz, and Orgel, *J.*, 1953, 3740). The absorption spectra of sodium phenoxide and disodium salicylate are also recorded in the Table. The spectrum of the former is in good agreement with that recently reported by Davies and Jones (*J.*, 1954, 120).

On the basis of these observations, therefore, it should be possible to distinguish between structures (I) and (II) (R = H). Thus a band due to phenolic OH at 3200—3500 cm.$^{-1}$ would not be expected for a compound (I) but is likely for a compound (II; R = H). Both compounds, however, are likely to show some broad absorption in the region 2500—3100 cm.$^{-1}$. Comparison of the spectra of methyl salicylate and sodium methyl salicylate and of sodium salicylate and disodium salicylate shows that in both cases replacement of the hydrogen, bonded to the carbonyl group, by sodium results in a shift of 10—14 cm.$^{-1}$. On this basis a compound of structure (I; R = H) can be expected to give a carbonyl absorption band near 1650 cm.$^{-1}$ whereas structure (II) would give a band near 1600 cm.$^{-1}$. Comparisons in the regions 1400—1465 and near 1250 cm.$^{-1}$ are not likely to be very diagnostic since both structures are likely to give bands in these regions. The presence of a band in the 900—940 cm.$^{-1}$ region is likely if (I) is the structure but not if it is (II).

Sodium phenoxide was carboxylated by three methods, (i) by heating " sodium phenyl carbonate " (Schmitt, *loc. cit.*) at 145° in a sealed tube, (ii) by direct pressure carboxylation at 125—135°, and (iii) by passing dry carbon dioxide through a phenolic solution of sodium phenoxide at 140° (cf. B.P. 384,619/1932). The absorption spectra of the products obtained by these procedures were all substantially similar to that of authentic mono-

sodium salicylate, and differed from that expected for a structure of type (I; R = H). The spectrum of the product obtained by method (ii) showed some weak absorption bands arising from the presence of small amounts of sodium carbonate and sodium hydrogen carbonate. These by-products could be removed in hot absolute acetone, the recovered product then possessing a spectrum closely similar to that of authentic monosodium salicylate. The carbonates arise from the presence of moisture which, despite rigorous drying of the starting materials, is picked up during the charging of the autoclave. In the other two methods moisture could more easily be excluded and only traces of carbonate were formed.

Schmitt (*loc. cit.*) showed that sodium phenoxide combines with an equimolecular amount of dry carbon dioxide at room temperature to form a compound which he considered to be sodium phenyl carbonate, $PhO{\cdot}CO_2Na$, and he postulated it as an intermediate in the carboxylation reaction. This compound, which is readily decomposed by water, completely dissociates at about 80° at atmospheric pressure (Tijmstra, *loc. cit.*). We have confirmed the fact that dry sodium phenoxide, when kept in contact with dry carbon dioxide for 7—10 days, takes up almost the theoretical quantity. Much of the absorbed carbon dioxide can be removed merely by applying a high vacuum and all can be removed at 80° *in vacuo*, sodium phenoxide being recovered unchanged. Since the material remains as a discrete microcrystalline powder during both the absorbing and the desorbing process, it is improbable that the crystal lattice undergoes sufficient distortion at room temperature to permit the large separation of the sodium and phenoxy-ions necessary for the formation of a new carbon–oxygen bond (as in $PhO{\cdot}CO_2Na$). It is known that sodium phenoxide readily forms chelate compounds with oxygenated substances, *e.g.*, with acetone (Segaller, *J.*, 1914, **105**, 114) and phenol (Gentsch, G.P. 156,761; *Chem. Zentr.*, 1905, I, 313); it is therefore likely that it will weakly chelate with carbon dioxide in a similar way. The infra-red absorption spectrum of the sodium phenoxide–carbon dioxide complex shows a medium-strength band, due to a carbonyl function, at 1684 cm.$^{-1}$. Sodium methyl carbonate, $MeO{\cdot}CO_2Na$, a stable recrystallisable solid, has an absorption band, due to carbonyl, at 1630 cm.$^{-1}$. Dimethyl carbonate and methyl phenyl carbonate possess carbonyl bands at 1748 and 1754 cm.$^{-1}$ respectively, indicating that the phenyl group has little effect on the position of the carbonyl band. These facts suggest that Schmitt's " sodium phenyl carbonate " is a complex which may be represented as (III). Davies (*Z. physikal. Chem.*, 1928, **134**, 57) has shown that this complex does not dissociate between 120° and 160° provided the pressure exceeds about 4 atmospheres.



(III)

Gilman, Arntzen, and Webb (*loc. cit.*) have suggested that, at the temperature of the Kolbe–Schmitt reaction, alkali-metal phenoxides tautomerise to the corresponding *ortho*-metallated structures and that these tautomers either react directly with carbon dioxide as does, for example, phenyl-lithium, or react with non-tautomerised alkali-metal phenoxide to produce *ortho*-metallated compounds which then react with carbon dioxide. Both of these views seem unlikely since it is well known that sodium phenoxide at temperatures above 120° reacts with alkyl halides to give, substantially, the corresponding alkyl phenyl ether (*e.g.*, Vincent, *Bull. Soc. chim.*, 1883, **40**, 106). We have confirmed this observation by adding *n*-hexyl bromide to sodium phenoxide at 150° and, by infra-red absorption analysis of the product, have shown it to contain at least 91% of *n*-hexyl phenyl ether. If tautomerism of sodium phenoxide had occurred at this temperature, appreciable quantities of *ortho*-substituted products should have been formed. Although benzyl chloride reacts with sodium phenoxide at 80° to give *ortho*-substituted products this is an anomalous reaction since diphenylmethyl bromide *ortho*-substitutes sodium phenoxide *even in the cold* (Claisen *et al.*, *Annalen*, 1925, **442**, 210). Moreover, Gilman *et al.* (*loc. cit.*) showed that treatment of lithium phenoxide with carbon dioxide at room temperature did not give any salicylic acid. The second view of Gilman and his collaborators is also disproved by the absence of any disodium salicylate in the carboxylation products.

The familiar effect of small amounts of water in reducing the extent of carboxylation in the Kolbe–Schmitt reaction may well be due to the stronger chelating power of water with

sodium phenoxide. Various authors (cf. Brady and Jakobovits, *J.*, 1950, 767) have commented on the specific effect of different alkali metals in carboxylation reactions, attributing it to differences in the chelating strengths of the metals. In this paper we have considered only the behaviour of sodium phenoxide but later we hope to deal with this phenomenon in more detail.

Phenol will only undergo carboxylation in the form of the alkali-metal phenoxide (Kolbe–Schmitt reaction) (cf. Kinney and Ward, *J. Amer. Chem. Soc.*, 1933, **55**, 3796). In the Marasse modification of the reaction (G.P. 73,279/1893) where the free phenol is heated with anhydrous potassium carbonate and carbon dioxide under pressure it has been shown that phenoxide formation is a necessary prelude to reaction (Wessely *et al.*, *loc. cit.*). It therefore seems likely that this type of carboxylation involves electrophilic attack on the *ortho*-carbon atom (cf. Seel, *loc. cit.*). Presumably, a similar process can operate when carboxylation is carried out in phenol solution; here, one of the phenol molecules of the sodium phenoxide–phenol solvate would be displaced by a molecule of carbon dioxide with subsequent electrophilic attack on the *ortho*-position.

Although the experimental results described above show that Tijmstra's formulation (*loc. cit.*) of the reaction product as sodium salicyloxide (I; R = H) is no longer tenable, this does not rule out the possibility that his original hypothesis of direct nuclear carboxylation may still represent the first step in the reaction, and that subsequent interchange of hydrogen and sodium ions (or atoms) occurs, giving sodium salicylate as the final product. However an alternative reaction mechanism, based on the preliminary association of sodium phenoxide with carbon dioxide under pressure to form a complex, and involving intramolecular reaction with displacement of the *ortho*-hydrogen by electrophilic attack, appears to us to offer a more satisfactory scheme of reaction. The absence of disodium salicylate in the carboxylation products, already described, strongly supports the intra-

Infra-red absorption bands (cm.$^{-1}$). (Disubstituted derivatives are all *o*-compounds.)

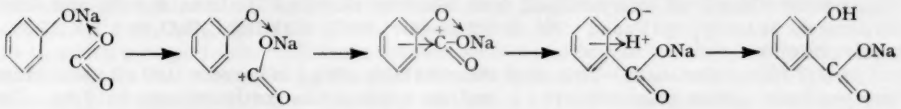
C_6H_4(OH)(CO$_2$Na)	C_6H_4(OH)(CO$_2$Me)	C_6H_4(ONa)(CO$_2$Me)	C_6H_4(OMe)(CO$_2$Na)	C_6H_4(OMe)(CO$_2$H)	C_6H_4(OH)(CO$_2$H)	C_6H_4(ONa)(CO$_2$Na)
—	~3400 m(sh)	—	—	—	—	—
—	3185 s	—	—	—	3255 m(sp)	—
—	3058 s(sh)	—	—	—	—	—
2925 s	2967 s	2905 s	2950 s	2910 s	2950 s	2905 s
2875 s(sh)	2857 m	2865 s(sh)	2890 s(sh)	2875 s(sh)	2890 s(sh)	2840 s(sh)
—	—	—	—	—	2740 m	—
—	—	—	—	—	2610 m	—
—	—	—	—	1689 s(sh)	1664 s	—
—	1675 s	1661 s	—	1669 s		
1600 s(sh)	—	—	1613 s	—	—	1590 m
—	1610 m	1597 m	1592 s	1595 m	1610 s	—
1585 s	1585 m	—	1577 s	1580 m	1582 m	—
—	—	—	1548 m(h)	—	—	1550 m
—	—	1536 m	—	—	—	1529 m

PhONa	Ph·CO$_2$Na	Ph·CO$_2$H	C_6H_4(CO$_2$H)(CO$_2$K)	Assignments
—	—	—	—	
—	—	—	—	OH (Bonded)
—	—	—	—	
2935 s	2915 s	2950 s	2900 s	
2875 s(sh)	2875 s(sh)	2905 s(sh)	2855 s(sh)	CH freqs. (from Nujol and compound *)
—	—	2690 m	—	Bonded OH submaxima
—	—	2575 m	—	
—	—	1692 s	1669 w	C=O of conjugated CO$_2$R (R = H or Me)
—	1600 s	—	1603 m(sh)	C=O of ionic CO$_2^-$
—	—	1605 m	—	
1585 s	—	1585 m	1587 m	Phenyl-ring vibrations
—	1553 s	—	1567 m	
1555 m	—	—	—	

s = strong band 80—100% of strongest band in spectrum. sh = shoulder.
m = medium „ 40—80% „ „ „ h = hump.
sp = sharp. b = broad band.

* The spectrum of methyl salicylate is that of the pure liquid.

molecular mechanism. The essential difference between the two mechanisms suggested appears to lie in the position of the displaced proton during the intermediate stage. According to the first mechanism a definite attachment of the proton to the carboxyl group as one stage of the reaction must be postulated, whereas, in the second, displacement of the proton on to the aromatic π-electron orbital (see below) would involve a close association of the proton with the aromatic nucleus during the intermediate stage. The latter mechanism will operate only if, in solid sodium phenoxide, the oxygen atom is coplanar with the benzene ring so that its " lone-pair " electrons can take part in a molecular π-electron orbital (cf. Coulson, " Valence," Oxford Univ. Press, 1952, p. 247). The reaction would then proceed according to the scheme outlined below (cf. Dewar, " The Electronic Theory of Organic Chemistry," Oxford Univ. Press, 1949, pp. 168, 227—228). In this case the proton held by the π-electron system would migrate to the phenolic oxygen.



That the assumption made is valid, at least for sodium phenoxide in solution, is implied in the observation that the ultra-violet absorption spectrum of sodium phenoxide in ethanol ($\lambda_{max.}$ 219, 273 mμ; log ε 3·4, 2·8) differs from that of benzene ($\lambda_{max.}$ 198, 256 mμ; log ε 3·9, 2·4) and approaches that of aniline ($\lambda_{max.}$ 233, 285 mμ; log ε 3·9, 3·2) (cf. Maccoll, *Quart. Reviews*, 1947, **1**, 45 and 56; Dewar, *op. cit.*, p. 201).

Experimental

Microanalyses were carried out by Miss M. Corner and her staff of this laboratory.

Infra-red Absorption Spectra.—Spectra were measured on a modified Hilger D 209 double-beam instrument (Hales, *J. Sci. Instr.*, 1949, **26**, 359; 1953, **30**, 52), the solid compounds being prepared as mulls in Nujol. Mulls of hygroscopic compounds were prepared in a " dry box." Compounds were prepared as follows.

Sodium Phenoxide.—(*a*) Clean sodium (4·6 g.) was converted into sodium sand in anhydrous sulphur-free toluene (300 ml.). Freshly distilled phenol (18·9 g.) in anhydrous toluene (50 ml.) was then added dropwise with stirring. After 4 hours' gentle refluxing the pasty mixture was allowed to cool and the product filtered off rapidly and washed with anhydrous toluene and finally with anhydrous ether. The snow-white powder was dried *in vacuo* in a desiccator (Found: C, 61·6; H, 4·8; Na, 19·95%; equiv., 116. Calc. for C_6H_5ONa: C, 62·1; H, 4·3; Na, 19·8%; equiv., 116). Ultra-violet absorption spectrum (in EtOH): $\lambda_{max.}$ 219, 273 mμ (log ε 3·4, 2·8). Microscopic examination (×600) of the product suspended in liquid paraffin showed it to consist of rectangular crystals.

(*b*) Commercial sodium phenoxide was recrystallised twice from boiling anhydrous acetone. Dried *in vacuo* (over P_2O_5), it was a white powder which gradually discoloured in a desiccator. Some samples prepared in this way melted at *ca.* 60° but resolidified at higher temperatures. This may have been due to traces of acetone (Found: Na, 20·0%). The infra-red absorption spectrum of the product was closely similar to that of the product obtained as in (*a*).

Sodium Salicylate.—Salicylic acid (1·38 g.; " AnalaR ") was dissolved in 0·1N-sodium hydroxide (100 ml.) and evaporated to dryness; the solid product was extracted (Soxhlet) with chloroform to remove traces of free acid and then dried at 100° (Found: C, 52·4; H, 3·45; Na, 14·6. Calc. for $C_7H_5O_3Na$: C, 52·5; H, 3·1; Na, 14·4%). The infra-red absorption spectrum of this compound was closely similar to that of a good-quality commercial sample.

Disodium Salicylate.—(*a*) Monosodium salicylate was neutralised with sodium hydroxide in water and the solution evaporated to dryness. Recrystallisation of the product from ethanol, washing with hot anhydrous acetone, and drying at 110° gave disodium salicylate (Found: Na, 25·7. Calc. for $C_7H_4O_3Na_2$: Na, 25·3%).

(*b*) Equimolecular quantities of sodium phenoxide and monosodium salicylate were heated at 240° *in vacuo* for 2 hr. The product was washed with anhydrous ether to remove phenol and with hot anhydrous acetone to remove unchanged starting materials. The product was dried at 150° *in vacuo* (Found: Na, 24·9%).

o-*Methoxybenzoic Acid.*—Prepared by Graebe's method (*Annalen*, 1905, **340**, 210), this had m. p. 102° (Found: C, 62·9; H, 5·0. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·3%).

Sodium o-Methoxybenzoate.—To *o*-methoxybenzoic acid (4 g.) in methanol (25 ml.) was added a solution of sodium hydroxide (1·05 g.) in methanol (15 ml.). The bulk of the methanol was removed under reduced pressure, anhydrous ether added, and the *sodium* salt filtered off, washed with ether, and dried at 110° *in vacuo* (P_2O_5) (Found: C, 55·0; H, 4·0; Na, 13·5. $C_8H_7O_3Na$ requires C, 55·2; H, 4·0; Na, 13·2%).

Sodium Methyl Salicylate.—To sodium (0·5 g.) dissolved in absolute methanol (25 ml.) was added a solution of freshly distilled methyl salicylate (3 g.) in methanol (25 ml.). After removal of the bulk of the methanol under reduced pressure, the solid product was filtered off and washed with cold absolute methanol, anhydrous ether, and finally boiling anhydrous benzene. It was dried at 120° *in vacuo* (Found: C, 55·2; H, 3·95; Na, 13·4. Calc. for $C_8H_7O_3Na$: C, 55·2; H, 4·0; Na, 13·2%).

Sodium Methyl Carbonate.—To a solution of sodium (1 g.) in absolute methanol (50 ml.) was added excess of solid carbon dioxide (10 g.) previously washed in methanol. The solid product was rapidly filtered off, recrystallised from absolute methanol (lustrous flakes), and dried *in vacuo* for 24 hr. (P_2O_5) (Found: Na, 24·0%; equiv., 98·0. Calc. for $C_2H_3O_3Na$: Na, 23·5%; equiv., 98·0).

Methyl Phenyl Carbonate.—To methyl chloroformate (40 g.) in benzene (100 ml.) was added dry powdered sodium phenoxide (17 g.), and the mixture was gently refluxed for 3 hr. The product recovered by distillation, after filtration from the sodium chloride, was redistilled, taken up in light petroleum (b. p. 40—60°), and filtered through a short column of alumina. Fractionation of the eluate gave methyl phenyl carbonate (10 g.), b. p. 120—121°/38 mm., $n_D^{18\cdot5}$ 1·4972 (Found: C, 63·35; H, 5·4. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·3%). The spectrum of this compound possessed an absorption band, due to carbonyl, at 1754 cm.$^{-1}$.

Other Compounds.—Salicylic acid was "AnalaR" material, recrystallised and resublimed as white needles, m. p. 160—161°.

Potassium hydrogen phthalate was "AnalaR" material, dried at 110°.

Benzoic acid was "AnalaR" material, m. p. 122°.

Sodium benzoate was of reagent grade (B.D.H.), dried at 110°.

Dimethyl carbonate was of reagent grade (B.D.H.). The spectrum of this compound possessed an absorption band due to carbonyl, at 1748 cm.$^{-1}$.

Kolbe–Schmitt Carboxylation Products.—(a) *Sealed tube technique.* A Carius tube containing dry sodium phenoxide (0·99 g.) was attached to a tube and tap system so that it could be successively evacuated and connected to a reservoir of dry carbon dioxide (dried over P_2O_5 for 72 hr.). After 96 hr. the theoretical amount of carbon dioxide (0·37 g.) had been absorbed. Dry air was admitted to the tube which was then sealed and heated for 2 hr. at 145°. After cooling, no large internal pressure was present. The product had a faint pink colour (Found: Na, 14·4. Calc. for $C_7H_5O_3Na$: N, 14·4%).

(b) *Autoclave technique.* A glass tube containing dry sodium phenoxide (1·98 g.) was placed in a steel autoclave (*ca.* 100 c.c.), and air was removed by flushing twice with carbon dioxide which had been dried for 72 hr. (P_2O_5) in a second autoclave (2 l.). The smaller autoclave was then filled with carbon dioxide at a pressure of 250 lb./sq. in. and heated at 125—135° for 3 hr. (1·25 hr. preheating). On opening of the autoclave it was found that some phenol (0·11 g.) had sublimed to the upper parts. The product (2·49 g.) was washed with a little anhydrous ether to give product (B). Part of this was treated with hot absolute acetone, and the soluble material (Found: Na, 13·8%) recovered by evaporating off the solvent at room temperature under reduced pressure. The infra-red absorption spectrum of the acetone-insoluble material showed it to be essentially a mixture of sodium carbonate and sodium hydrogen carbonate.

(c) *Carboxylation in phenol solution (method of* B.P. 384,619). Solid sodium hydroxide (0·41 g.) was dissolved in freshly distilled phenol (21 g.) by heating it at 140° with passage of dry nitrogen. The excess of water was removed azeotropically by distillation with dry xylene (30 ml.). Dry carbon dioxide was then passed briskly through the melt held at 140—150° for 14 hr. The product (1·24 g.) was recovered by addition of anhydrous ether, filtration, and thorough washing with ether.

Sodium Phenoxide–Carbon Dioxide Complex.—A tube containing dry, finely powdered sodium phenoxide (551 mg.) was evacuated and then connected to a reservoir of carbon dioxide which had been dried for several weeks (P_2O_5). After 7 days at room temperature 88% (183 mg.) of the theoretical amount of carbon dioxide had been absorbed. Standing in contact with carbon dioxide for a further 3 days led to no further absorption.

A mull of this complex in Nujol, prepared in a "dry box," showed a medium-strength band due to carbonyl at 1684 cm.$^{-1}$.

A sample of the sodium phenoxide–carbon dioxide complex prepared in a similar way was subjected cautiously to a vacuum of 0·05 mm. of mercury. The powder became disturbed as it " degassed." The containing vessel was immersed in boiling benzene vapour and the vacuum of 0·05 mm. maintained for 3 hr. The residual powder possessed a spectrum closely similar to that of the original sodium phenoxide, and still appeared microcrystalline on microscopic examination.

Reaction of n-*Hexyl Bromide with Sodium Phenoxide.*—To dry, finely powdered sodium phenoxide (5·0 g.), heated at 160° for 30 min., was added *n*-hexyl bromide (50 ml.), and the mixture was refluxed for 8 hr. The solid sodium bromide (4·5 g.; theor., 4·4 g.) was filtered off and washed well with anhydrous ether. Extraction of the bulked ethereal filtrates with 20% sodium hydroxide solution led to the recovery, in the usual way, of a phenolic product (*a*) (0·25 g.) which partly crystallised. Distillation removed ether and unchanged *n*-hexyl bromide from the dried ethereal solution and gave the main product (*b*), b. p. 235—245° (6·55 g., 90·8%), leaving a still residue (*c*) (0·70 g.). Refractionation of (*b*) gave a good sample of *n*-hexyl phenyl ether, b. p. 240—241°, n_D^{20} 1·4928 (Found: C, 80·6; H, 10·1. Calc. for $C_{12}H_{18}O$: C, 80·9; H, 10·1), which gave no colour with ferric chloride solution. For *n*-hexyl phenyl ether Hurd and McNamee (*J. Amer. Chem. Soc.*, 1932, **54**, 1648) give b. p. 125—128°/10 mm., n_D^{25} 1·4889. The infra-red absorption spectrum of this compound had a broad similarity to that of anisole, and possessed strong absorption bands at 1079 and at 1250 cm.$^{-1}$ indicative of the ether linkage (Tschamler and Leutner, *Monatsh.*, 1952, **83**, 1502). Examination of the spectrum of product (*b*) showed it to be substantially the same product. Residue (*c*) contained unidentified impurities in addition to *n*-hexyl phenyl ether, while phenolic fraction (*a*) consisted largely of unchanged phenol.

We are indebted to Dr. Mansel Davies, University College of Wales, Aberystwyth, for helpful comments on the infra-red spectra and to Mr. W. Kynaston for assistance with their measurement. The work formed part of the programme of the Chemical Research Laboratory and is published by permission of the Director.

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Substituted Anthracene Derivatives. Part VII. An Examination of Some Naphthacene* endo*Oxide Derivatives.*

By G. M. BADGER, R. S. PEARCE, H. J. RODDA, and I. S. WALKER.

[Reprint Order No. 5212.]

Several compounds with postulated structures (*e.g.*, IV, V, VI) involving transannular mono-oxide bridges have been examined.

Bergmann's compound (supposedly VI) has been identified as *o*-dibenzoylbenzene.

It has been confirmed that the original rubrene skeleton (I) is retained in rubrene mono-oxide (IV) and that the three oxides of rubrene have similar absorption spectra. On the other hand, the original rubrene skeleton is not present in rubrene *iso*oxide, for it is reduced by iron and acetic acid to the phenoxytriphenylnaphthacene (XIV). Other degradations of rubrene *iso*-oxide have also been investigated and the structure (X) is now proposed for this substance. Tetra-*p*-tolylnaphthacene *iso*oxide (" tetramethylrubrene *iso*-oxide ") has been synthesised and reduced with magnesium and methylmagnesium iodide to 5 : 6 : 11-tri-*p*-tolylnaphthacene and *p*-cresol.

THE bright red hydrocarbon rubrene (5 : 6 : 11 : 12-tetraphenylnaphthacene) (I; Ar = Ph) forms three oxides. When irradiated in the presence of molecular oxygen, it forms a photo-oxide having a transannular peroxide structure (II; Ar = Ph) (Dufraisse, *Bull. Soc. chim.*,

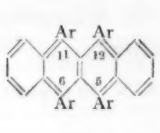
* Part VI, *J.*, 1952, 1175.

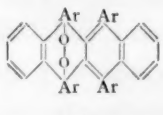
1939, **6**, 422). This structure seems to be established, more especially by the observation that the photo-oxide is reduced, on catalytic hydrogenation, to the *cis*-diol (III; Ar = Ph) (Dufraisse and Houpillart, *Compt. rend.*, 1937, **205**, 740). When rubrene is oxidised with dilute nitric acid or with certain other oxidising agents, however, a mono-oxide is formed (Moureu, Dufraisse, and Enderlin, *ibid.*, 1929, **188**, 1528), which is also obtained by reduction of the photo-oxide with zinc and acetic acid (Dufraisse and Enderlin, *Bull. Soc. chim.*, 1932, **51**, 132) and by thermal dehydration of the *cis*-diol (III; Ar = Ph) (Enderlin, *Ann. Chim.*, 1938, **10**, 5). The endocyclic mono-oxide structure (IV) has been proposed for this substance (Enderlin, *loc. cit.*; *Compt. rend.*, 1936, **202**, 669). Similar mono-oxides have been obtained from rubrene derivatives (Enderlin, *loc. cit.*), but it is noteworthy that no such oxide of 9 : 10-diphenylanthracene could be obtained by direct oxidation, by partial reduction of the photo-oxide, or by thermal dehydration of the 9 : 10-diol (Dufraisse and Le Bras, *Bull. Soc. chim.*, 1937, **4**, 349, 1037).

The *iso*oxide of rubrene is obtained by isomerisation of the photo-oxide with magnesium iodide (Dufraisse and Badoche, *Compt. rend.*, 1930, **191**, 104). The structure (V) was proposed for this (Enderlin, *loc. cit.*, 1938; *Compt. rend.*, 1936, **203**, 192) and received some support from the facts that such isomerisations are known only in the *meso*-tetra-arylnaphthacene series, and that 9 : 10-diphenylanthracene photo-oxide does not isomerise (Dufraisse and Le Bras, *Bull. Soc. chim.*, 1937, **4**, 349).

It has already been pointed out (Badger and Pearce, *J.*, 1950, 2311) that although transannular dioxides (such as II) are little strained (see also Dufraisse, *loc. cit.*, 1939), a mono-oxide bridge as in (IV or V) involves considerable distortion of the normal valency angles for oxygen and carbon and of the normal oxygen–carbon bond length. For this reason, it was thought desirable to re-investigate the oxides of rubrene and its derivatives. As part of the same investigation, the supposed transannular mono-oxide (VI) obtained by Bergmann (*J.*, 1938, 1147) has also been re-examined.

Bergmann obtained the Diels–Alder adduct (VII; Ar = Ph) from 1 : 4-naphthaquinone and 1 : 3-diphenyl*iso*benzofuran, and treated this with hydrobromic acid in acetic acid. Part of the material was dehydrated to the known 6 : 11-diphenylnaphthacene-5 : 12-quinone (XIII); but a colourless compound was also obtained. From the analytical figures, and by analogy with some work of Diels, Alder, and Stein (*Ber.*, 1929, **62**, 2337),


(I)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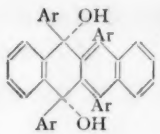
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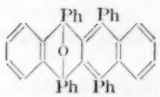
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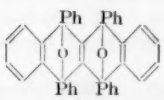
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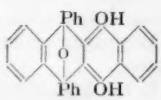
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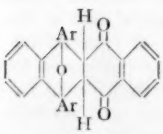
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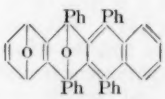
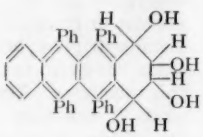

(VIII)


(IX)

Bergmann concluded that some of the adduct had enolised, and he therefore assigned the structure (VI) to his product. It has now been found, however, that the colourless substance obtained in this way is far too stable to have the structure indicated, and it has been identified as *o*-dibenzoylbenzene. The Diels–Alder reaction is, of course, reversible, and

the *o*-dibenzoylbenzene is probably formed by aerial oxidation of the diphenyl*iso*benzofuran which is obtained by partial dissociation of the adduct into its components.

However, the (other) three rubrene oxides are undoubtedly derivatives of naphthacene, and their properties are known in some detail (Dufraisse, *loc. cit.*, 1939; Enderlin, *loc. cit.*, 1938).

For example, rubrene mono-oxide is reduced to rubrene by iron and acetic acid (Moureu *et al.*, and Dufraisse and Enderlin, *locc. cit.*) and by methylmagnesium iodide and excess of magnesium (present work). Moreover, it showed no hydroxyl absorption in the infra-red. The structure (IV) therefore seems to be established in spite of the steric distortion.

Enderlin's structure (V) for the *iso*oxide can be quickly dismissed, for the absorption spectrum of the *iso*oxide is almost identical with that of rubrene mono-oxide and of rubrene photo-oxide (Fig. 1), indicating that the three compounds have the same chromophore. While this work was in progress, the same conclusion was reached by Gillet (*Compt. rend.*, 1949, **229**, 936; *Bull. Soc. chim.*, 1950, **17**, 1141), who also pointed out that all three spectra resemble that of 1 : 4-diphenylnaphthalene. Gillet concluded that this conjugated system must be present in all three rubrene oxides : he proposed structure (VIII) for the *iso*oxide. This also seems to be erroneous : it includes an unhindered ethylenic double bond and would therefore be expected to show the usual double-bond reactivity, but in fact, rubrene *iso*oxide does not react with osmium tetroxide under the usual conditions. Rubrene mono-oxide and photo-oxide are also unreactive towards osmium tetroxide, but rubrene itself behaves as an ordinary reactive aromatic hydrocarbon (such as anthracene; see Cook and Schoental, *Nature*, 1948, **161**, 237). Osmium tetroxide added to the 1 : 2- and 3 : 4-bonds, for 1 : 2 : 3 : 4-tetrahydro-1 : 2 : 3 : 4-tetrahydroxyrubrene (IX) was isolated after hydrolysis of the complex. The structure of this tetrol is confirmed by its absorption spectrum, which is of the general " anthracene " type.

When the *iso*oxide is treated with a large excess of magnesium and methylmagnesium iodide, 5 : 6 : 11-triphenylnaphthacene (XI) and phenol are obtained in almost quantitative yield (Dufraisse and Badoche, *Compt. rend.*, 1931, **193**, 242; Badoche, *Bull. Soc. chim.*, 1936, **3**, 2040). This suggests that the two oxygen atoms are not bound in the same way. This reaction has been confirmed, and the structure of the triphenylnaphthacene (XI) established unequivocally by synthesis. For this purpose diphenylnaphthacenequinone (XIII) was reduced to the diphenylbenzanthrone (XII), which by treatment with phenylmagnesium bromide and subsequent dehydration gave 5 : 6 : 11-triphenylnaphthacene (XI).

To be able to perform this degradation on the *iso*oxide of a rubrene derivative having substituents in the four phenyl rings, the synthesis of 5 : 6 : 11 : 12-tetra-*p*-tolylnaphthacene (I; Ar = *p*-tolyl) was undertaken. 1 : 4-Naphthaquinone and 1 : 3-di-*p*-tolyl*iso*benzofuran, gave the adduct (VII; Ar = *p*-tolyl), which was then dehydrated with ice-cold sulphuric acid to 6 : 11-di-*p*-tolylnaphthacene-5 : 12-quinone (cf. Bergmann, *loc. cit.*; Dufraisse and Compagnon, *Compt. rend.*, 1938, **207**, 585). This with *p*-tolyl-lithium gave the *cis*-diol (III; Ar = *p*-tolyl), which was reduced with iron and acetic acid to the desired " tetramethylrubrene " (I; Ar = *p*-tolyl) (cf. Allen and Gilman, *J. Amer. Chem. Soc.*, 1936, **58**, 937; Dufraisse and Velluz, *Compt. rend.*, 1935, **201**, 1394; *Bull. Soc. chim.*, 1936, **3**, 1905). It is of interest that an attempt to dehydrate the *cis*-diol by heat in *vacuo* resulted only in isomerisation, the *trans*-diol being obtained. The new derivative has a visible absorption spectrum almost identical with that of rubrene (cf. Badger and Pearce, *Spectrochim. Acta*, 1951, **4**, 280) except that the intense band in the ultra-violet is at a longer wavelength. The photo-oxide (II; Ar = *p*-tolyl) was obtained in the usual way, and on isomerisation with magnesium iodide gave the *iso*oxide, the absorption spectrum of which was almost identical with that of rubrene *iso*oxide (cf. Fig. 1).

When tetra-*p*-tolylnaphthacene *iso*oxide was reduced with excess of magnesium and methylmagnesium iodide, 5 : 6 : 11-tri-*p*-tolylnaphthacene was obtained, together with *p*-cresol. This isolation of the *p*- rather than of *m*-cresol excludes the possibility that the *iso*oxides contain an oxygen bridge between the 11(or 12)-position and a position in a phenyl group which is *meta* to the methyl substituent. The absorption spectrum of the tri-*p*-tolylnaphthacene was similar to that of triphenylnaphthacene (see Table; cf. Badoche, *loc. cit.*).

A hydroperoxide structure for the *iso*oxides would account for the observed results in this reaction ; but rubrene *iso*oxide shows none of the reactions of a hydroperoxide. It is stable to heat, contains no active hydrogen, and has no hydroxyl absorption in the infra-red.

The reducing action of magnesium and methylmagnesium iodide is identical with that of the Gomberg–Bachmann reagent (Mg + MgI_2), for dissociation occurs according to the equations, $2MeMgI + Mg \rightleftharpoons Me_2Mg + MgI_2 + Mg \rightleftharpoons Me_2Mg + 2MgI$ (Allen and Bell, *J. Amer. Chem. Soc.*, 1940, **62**, 2408; Kharasch and Weinhouse, *J. Org. Chem.*, 1936, **1**, 209; Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1927, **49**, 236, 2548; 1928, **50**, 2762). It is very unlikely that this reagent could bring about the fission of a carbon–carbon bond. The reduction of the *iso*oxides to triarylnaphthacene and a phenol therefore seems to indicate that the *iso*oxide contains a phenoxy-group, and this has been confirmed by the finding that cold concentrated sulphuric acid, or fusion with potassium hydroxide converts rubrene *iso*oxide into phenol and the triphenylbenzanthrone (XVII). The structure of this product

FIG. 1. *Absorption spectra of rubrene monooxide* (———), isooxide (. . . . .), *and photo-oxide* (– – – – –), *in ethanol.*

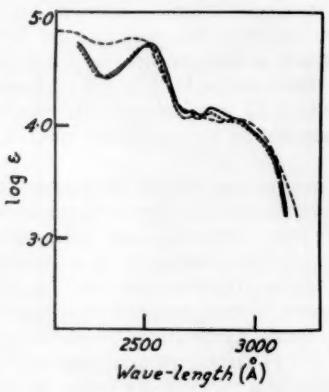
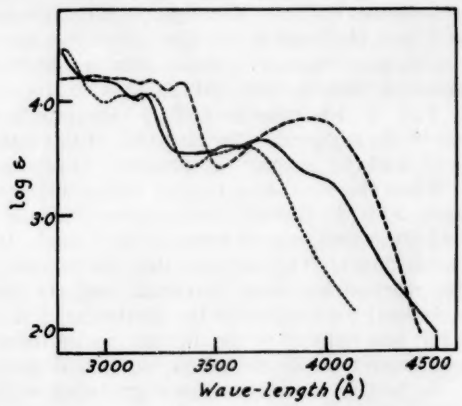


FIG. 2. *Absorption spectra of* (———) *diphenylbenzanthrone* (XII), (– – – – –) *triphenylbenzanthrone* (XVII), *and* (. . . . .) *hydroxytriphenylbenzanthrone* (XV), *in benzene.*



is supported by its absorption spectrum (Fig. 2), which is very similar to that of the diphenylbenzanthrone (XII).

Reduction of rubrene *iso*oxide with iron and acetic acid gave a compound which had the same appearance and m. p. as rubrene and gave no m. p. depression when mixed with it (cf. Enderlin, *loc. cit.*, 1938; Dufraisse and Badoche, *loc. cit.*, 1930). However, its empirical formula was $C_{42}H_{28}O$. Its absorption spectrum (see Table) was almost identical

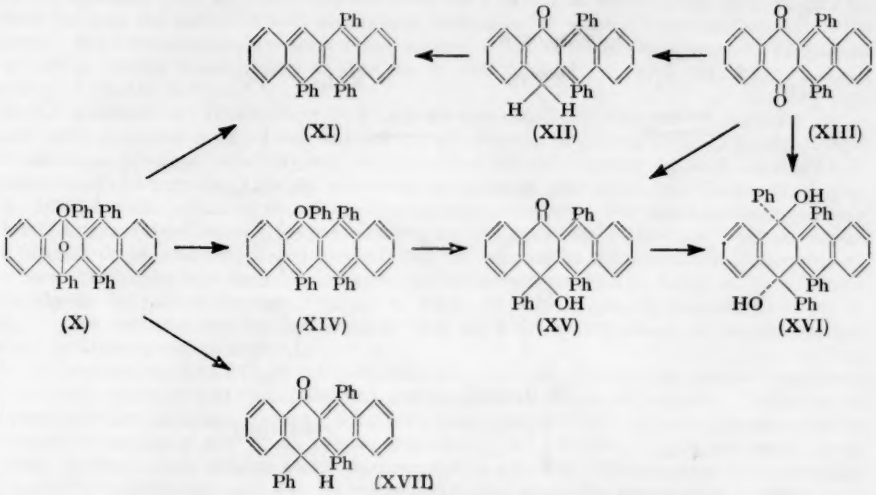
Absorption maxima (Å) *and intensities* (*log* ε) (*in parentheses*) *of naphthacene derivatives in benzene.*

	Band : *	A	C	D	E
Rubrene		3030 (5·07)	4650 (3·79)	4950 (4·07)	5300 (4·08)
5 : 6 : 11 : 12-Tetra-*p*-tolylnaphthacene		3040 (5·12)	4640 (3·79)	4940 (4·07)	5300 (4·11)
5 : 6 : 11-Triphenylnaphthacene (XI)		2950 (5·02)	4450 (3·64)	4730 (3·93)	5050 (4·06)
5 : 6 : 11-Tri-*p*-tolylnaphthacene		2960 (5·06)	4450 (3·75)	4730 (4·05)	5060 (4·10)
5-Phenoxy-6 : 11 : 12-triphenylnaphthacene (XIV)		2990 (5·04)	4600 (3·77)	4900 (4·05)	5250 (4·08)

* The nomenclature is that used by Badger and Pearce (*Spectrochim. Acta*, 1951, **4**, 280).

with that of rubrene, except that the absorption bands were shifted about 50 Å to shorter wave-lengths. It showed no hydroxyl absorption in the infra-red. It must therefore be 5-phenoxy-6 : 11 : 12-triphenylnaphthacene (XIV). On oxidation with hot dilute nitric acid, or with cold dilute permanganate, it gave the hydroxytriphenylbenzanthrone

(XV), under the conditions in which rubrene is oxidised almost exclusively to the mono-oxide (Moureu *et al.*, *loc. cit.*). The structure of this hydroxytriphenylbenzanthrone follows from its absorption spectrum (Fig 2) and from its synthesis from 6 : 11-diphenylnaphthacene -5 : 12-quinone (XIII) by treatment with one mol. of phenylmagnesium bromide. Moreover, when the hydroxytriphenylbenzanthrone (XV) was treated with phenylmagnesium



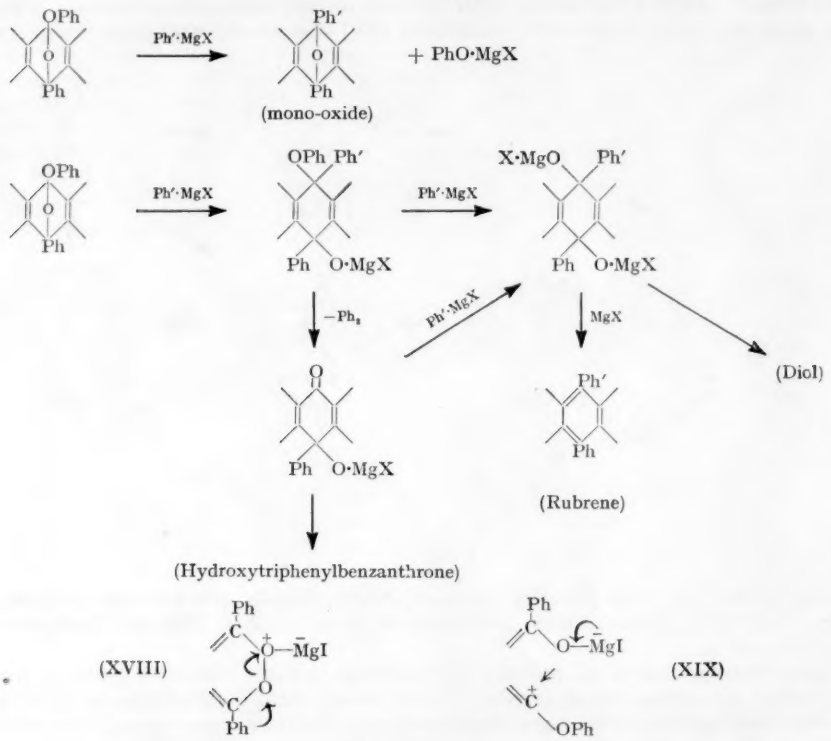
bromide, it was converted into the *trans*-diol (XVI). Finally, the infra-red spectrum of the hydroxytriphenylbenzanthrone, in chloroform, gave a band at 3540 cm.$^{-1}$ indicative of a hydroxy-group.

These transformations all indicate that rubrene *iso*oxide contain a phenoxy-group. And further, as rubrene *iso*oxide is reduced to the phenoxytriphenylnaphthacene (XIV) with iron and acetic acid, under the same conditions in which rubrene mono-oxide (IV) is reduced to rubrene, it seems that the *iso*oxide must have the structure (X). This accounts for its absorption spectrum (Fig. 1) and for all the known reactions.

The fundamental carbon skeleton of rubrene is not retained in this structure for rubrene *iso*oxide, which, at first, seemed to be at variance with Dufraisse's contention (*Bull. Soc. chim.*, 1933, **53**, 789) that the *iso*oxide may be reduced to rubrene, to rubrene mono-oxide, and to the diol (XVI) by treatment with (filtered) Grignard reagents. No experimental details seem to have been published on this work, which has accordingly been repeated. Although the products named could not be isolated from any single reaction mixture, the results have, nevertheless, been substantially confirmed. With 15—20 mols. of phenylmagnesium bromide, rubrene *iso*oxide was converted into rubrene; with 2 mols., rubrene mono-oxide was obtained; and with 1·5 mols., the hydroxytriphenylbenzanthrone (XV). As it has been shown that this substance is converted into the *trans*-diol by treatment with phenylmagnesium bromide, Dufraisse's statement is confirmed. This, however, does not prove that the fundamental carbon skeleton of rubrene is retained in the *iso*oxide. On the contrary, by analogy with the splitting of aryl allyl ethers with methylmagnesium iodide (Meltzer and King, *J. Amer. Chem. Soc.*, 1953, **75**, 1355), the products would be *expected*, the reactions being those indicated in the annexed partial formulæ.

In considerations of the mechanism of the isomerization of rubrene photo-oxide (II; Ar = Ph) to rubrene *iso*oxide (X), we wish to acknowledge the benefit of helpful discussions with Professors Melvin S. Newman and R. B. Woodward. It is suggested that the magnesium iodide first co-ordinates with one oxygen of the photo-oxide, iodine being liberated, and that the resulting complex subsequently rearranges (see XVIII). Experimentally the reaction mixture takes on a brown iodine-like colour. The carbon atom now has a

positive charge so that cyclisation occurs (see XIX) to give the *iso*oxide (X) with liberation of the magnesium, and re-formation of the magnesium iodide.



Experimental

Bergmann's Compound.—The Diels–Alder adduct was obtained from 1 : 3-diphenyl*iso*benzofuran and 1 : 4-naphthaquinone, and after treatment with acetic and hydrobromic acid at 37° for 2 days, two products were isolated as described by Bergmann (*loc. cit.*). One was identified as the known yellow diphenylnaphthacenequinone in agreement with Bergmann, and the second was obtained in colourless needles, m. p. 149—150° (Bergmann gives m. p. 150°).

The colourless product dissolved in cold concentrated sulphuric giving a red colour, and was recovered unchanged on dilution with water. It was recovered unchanged after attempted oxidation with chromic acid in glacial acetic acid. On refluxing with zinc and acetic acid, the solution became yellow and exhibited an intense bluish-green fluorescence identical with that given by 1 : 3-diphenyl*iso*benzofuran. The mixed m. p. with *o*-dibenzoylbenzene showed no depression, and the substance was further characterised by the formation of 1 : 4-diphenylphthalazine, m. p. and mixed m. p. 192°, from hydrazine hydrate in boiling alcohol. Bergmann's analytical figures agree with those for *o*-dibenzoylbenzene (Found : C, 83·9; H, 4·9. Calc. for $C_{20}H_{24}O_2$: C, 83·9; H, 4·9%).

Reduction of Rubrene Mono-oxide with Magnesium and Methylmagnesium Iodide.—Rubrene mono-oxide (500 mg.) was shaken for 8 days with the Grignard reagent, prepared from magnesium (4 g.), methyl iodide (8 g.) and ether (50 c.c.). The resulting dark solution was poured on cracked ice, and the mixture steam-distilled. The distillate contained no phenol. The red residue was extracted from the aqueous suspension with benzene, and after drying and evaporation to small volume this deposited red crystals of rubrene, identified by m. p. and absorption spectrum.

Addition of 1 : 3-*Di*-p-*tolyliso*benzofuran *to* 1 : 4-*Naphthaquinone.*—An intimate mixture of

1 : 3-di-*p*-tolyl*iso*benzofuran (23·6 g.; Guyot and Vallette, *Ann. Chim.*, 1911, **23**, 363) and 1 : 4-naphthaquinone (12·5 g.) was moistened with chloroform. The mixture immediately became black, but after a few minutes white. A little ether was then added. After 1 hr. the solid was collected and recrystallised from ethyl acetate. The *adduct* (30 g., 86%) formed colourless flat rectangular crystals, m. p. 163° (Found: C, 84·4; H, 5·3. $C_{32}H_{24}O_3$ requires C, 84·2; H, 5·3%).

6 : 11-*Di*-p-*tolylnaphthacene*-5 : 12-*quinone*.—The adduct (27 g.) was dissolved in concentrated sulphuric acid (150 c.c.) at −10°, and set aside for 1 hr. The solution was then poured on cracked ice, and the excess of acid neutralised with aqueous alkali; this also flocculated the quinone. After recrystallisation from ethyl acetate, 6 : 11-*di*-p-*tolylnaphthacene*-5 : 12-*quinone* (15 g., 58%) formed lemon-yellow needles, m. p. 288° (Found: C, 87·3; H, 4·9. $C_{32}H_{22}O_2$ requires C, 87·6; H, 5·1%).

cis-5 : 12-*Dihydro*-5 : 12-*dihydroxy*-5 : 6 : 11 : 12-*tetra*-p-*tolylnaphthacene*.—A solution of *p*-tolyl-lithium, prepared from *p*-bromotoluene (61 g.), lithium (6 g.) and ether (1 l.) and filtered under nitrogen pressure, was refluxed, the returning liquid dropping on to 6 : 11-di-*p*-tolyl-naphthacene-5 : 12-quinone (13 g.) in a Soxhlet thimble (cf. Bachmann and Chemerda, *J. Org. Chem.*, 1939, **4**, 583). After 9½ hr., all the quinone had dissolved. Heating was continued for a further 2½ hr., and the mixture then poured on 1½ kg. of cracked ice. The ether layer was separated, filtered, dried, and evaporated to small volume, whereupon the crystalline *diol* separated. After recrystallisation from benzene, it formed colourless prisms (15·5 g., 84%), m. p. indefinite, depending on the rate of heating (Found: C, 89·1; H, 6·3. $C_{46}H_{38}O_2$ requires C, 88·7; H, 6·15%). This diol was not reduced when shaken for 8 days with excess of magnesium and ethereal methylmagnesium iodide.

6 : 11-*Di*-p-*tolyl*-5 : 6-11 : 12-*ditolylenenaphthacene*.—In one attempt to prepare the above diol, the crude product was steam-distilled and then added to hot *n*-propanol. Dehydration took place, and the colourless, sparingly soluble 6 : 11-*di*-p-*tolyl*-5 : 6-11 : 12-*ditolylenenaphthacene* was formed, having m. p. 402° (from xylene) (Found: C, 94·1; H, 5·8. $C_{46}H_{34}$ requires C, 94·2; H, 5·8%), giving a very intense violet fluorescence in solution. Dehydration of rubrenediol gives a similar hydrocarbon (see, *e.g.*, Dufraisse and Velluz, *Bull. Soc. chim.*, 1936, **3**, 1905).

trans-5 : 12-*Dihydro*-5 : 12-*dihydroxy*-5 : 6 : 11 : 12-*tetra*-p-*tolylnaphthacene* (?).—In an attempt to prepare the mono-oxide, the *cis*-diol (500 mg.) was heated *in vacuo* at 260° for 30 min. After cooling, the pink brittle solid was recrystallised from benzene and the product, which seems to be the trans-*diol*, was obtained as colourless needles, m. p. 305° (Found: C, 88·9; H, 6·3%). It gave an intense colour with concentrated sulphuric acid.

5 : 6 : 11 : 12-*Tetra*-p-*tolylnaphthacene*.—A finely powdered intimate mixture of the *cis*-diol (5 g.) and iron powder (40 g.) was refluxed for 1 hr. in purified glacial acetic acid (500 c.c.), then poured into cold water (5 l.) and set aside for 3 hr. The solid was collected, dried, and extracted with benzene in a Soxhlet apparatus, in a dark room. The benzene solution was evaporated to small volume and the hydrocarbon obtained in 83% yield. After recrystallisation from benzene, 5 : 6 : 11 : 12-*tetra*-p-*tolylnaphthacene* formed short red prisms, m. p. 325° (Found: C, 93·7; H, 6·2. $C_{46}H_{36}$ requires C, 93·8; H, 6·2%). Solutions of this hydrocarbon were very rapidly photo-oxidised on exposure to light and air, and the solid itself was slowly photo-oxidised on exposure in thin layers to the ordinary light of the laboratory. In the latter respect it differs from rubrene.

5 : 6 : 11 : 12-*Tetra*-p-*tolylnaphthacene* 6 : 11-*Photo-oxide*.—A stream of oxygen was passed into a solution of tetra-*p*-tolylnaphthacene (1 g.) in benzene (1 l.) in direct sunlight. After a few minutes the solution became colourless, and was then evaporated to small volume. After recrystallisation from ether, the *photo-oxide* formed colourless prisms, m. p. 223° after preliminary reddening [Found: C, 87·35; H, 6·2. $C_{46}H_{36}O_2,\frac{1}{2}C_4H_{10}O$ requires C, 87·6; H, 6·3%). Rubrene photo-oxide also crystallises with ½ molecule of ether (Moureu, Dufraisse, and Gerard, *Compt. rend.*, 1928, **186**, 1027).

5 : 6 : 11 : 12-*Tetra*-p-*tolylnaphthacene* iso*Oxide*.—A solution of magnesium iodide was prepared by allowing iodine (3 g.) and excess of magnesium turnings to react in anhydrous ether (200 c.c.). The clear solution was cooled in an ice-bath and then added to an ice-cold solution of the photo-oxide (2 g.) in anhydrous benzene (150 c.c.). The mixture was kept in an ice-bath for 5 min., and then poured on cracked ice, and the organic layer was separated, washed with sodium thiosulphate solution, dried, and evaporated. Recrystallisation from ether gave 5 : 6 : 11 : 12-*tetra*-p-*tolylnaphthacene* iso*oxide* as colourless hexagonal plates, m. p. 198° (Found: C, 89·0; H, 5·8%. $C_{46}H_{36}O_2$ requires C, 89·0; H, 5·85%).

5 : 6 : 11-*Tri*-p-*tolylnaphthacene*.—The above *iso*oxide (0·5 g.) was shaken with a Grignard solution prepared from methyl iodide (10 g.), magnesium turnings (4 g.) and anhydrous ether

(100 c.c.) for 8 days. The whole was then poured on cracked ice and steam-distilled, and the ether layer of the distillate separated and combined with a second ethereal extract of the aqueous distillate. The combined extracts were evaporated, and the residue was heated with aqueous sodium hydroxide (0·4 c.c.; 33%) and aqueous chloroacetic acid (0·24 c.c.; 50%) for 1 hr. on a water-bath. After cooling, it was diluted slightly and acidified to pH 5 with hydrochloric acid. The liberated acid was taken up in ether (10 c.c.), extracted with aqueous sodium carbonate, and reprecipitated with hydrochloric acid. Recrystallisation from water gave colourless needles, m. p. 138° alone or mixed with an authentic specimen (m. p. 138°) of *p*-tolyloxyacetic acid. The material which was not volatile in steam was extracted with benzene, the resulting solution being orange-red with an intense green fluorescence. After evaporation, the product was collected and recrystallised from benzene–light petroleum. The 5 : 6 : 11-*tri*-p-*tolylnaphthacene* was formed as orange-red prisms, m. p. 244° (Found: C, 93·8; H, 6·4. $C_{39}H_{30}$ requires C, 93·9; H, 6·1%).

Rubrene iso*Oxide.—Test for ethylenic double bond.* Pyridine (3 drops) and a benzene solution of osmium tetroxide (0·4 c.c.; 10%) were added to a solution of rubrene *iso*oxide (15 mg.) in benzene (0·5 c.c.). No change of colour was apparent after 3 days. Tetramethylrubrene *iso*-oxide likewise showed no colour change, although ethylenic substances (*e.g.*, stilbene) reacted immediately with the formation of a brown colour or precipitate. Rubrene mono-oxide and rubrene photo-oxide also gave no colour change.

Oxidation of Rubrene with Osmium Tetroxide.—A suspension of rubrene (1·5 g.) in benzene (40 c.c.) and pyridine (0·5 c.c.) was treated with osmium tetroxide (1 g.) in benzene (10 c.c.). The colour darkened and the yellow fluorescence diminished immediately. After 3 days the mixture was diluted with light petroleum, and the brown solid collected, dissolved in methylene chloride (200 c.c.), and shaken with 1% aqueous potassium hydroxide (200 c.c.) containing mannitol (20 g.). After 3 hr., the organic layer, which was light yellow, was separated and evaporated. Recrystallisation from benzene gave the 1 : 2 : 3 : 4-*tetrahydro*-1 : 2 : 3 : 4-*tetrahydroxy*-5 : 6 : 11 : 12-*tetraphenylnaphthacene* (1·0 g.) as very small yellow prisms, m. p. 250° with decomposition (Found: C, 83·5; H, 5·7. $C_{42}H_{32}O_4$ requires C, 84·0; H, 5·4%).

1 : 4-*Diphenyl*-2 : 3-*benzanthrone* (XII).—A suspension of finely divided 6 : 11-diphenylnaphthacene-5 : 12-quinone (XIII; Dufraisse and Compagnon, *Compt. rend.*, 1938, **207**, 585) in glacial acetic acid (150 c.c.) was boiled with granulated tin (9 g.). The quinone gradually dissolved to a red solution, which faded to brown when the reduction was complete (10—15 hr.). The hot solution was filtered and concentrated to half its volume, and concentrated hydrochloric acid (10 c.c.) was added, whereupon the crude product crystallised. After purification by chromatography on alumina from benzene solution, and recrystallisation from 1 : 1 benzene–light petroleum (b. p. 90—120°) 1 : 4-*diphenyl*-2 : 3-*benzanthrone* (XII) (2·75 g.) was obtained as yellow prisms, m. p. *ca.* 260° depending on the rate of heating (Found: C, 90·8; H, 5·1. $C_{30}H_{20}O$ requires C, 90·8; H, 5·1%).

5 : 6 : 11-*Triphenylnaphthacene.*—A 0·4M-solution of phenylmagnesium iodide in ether (13 c.c.) and anhydrous benzene (60 c.c.) was boiled under reflux, 1 : 4-diphenyl-2 : 3-benzanthrone (1·0 g.) being suspended in a Soxhlet thimble under the condenser. After 24 hr. the red solution was poured on cracked ice and concentrated hydrochloric acid (20 c.c.). The organic layer was shaken for a few minutes with concentrated hydrochloric acid (4 × 25 c.c.), washed with distilled water, dried (Na_2SO_4), and evaporated to small volume. The resulting semi-solid mass was purified by chromatography on alumina, from benzene solution. Elution of the orange band, followed by evaporation and recrystallisation from benzene, gave 5 : 6 : 11-triphenylnaphthacene (0·35 g., 30%) as orange crystals, m. p. 175° unchanged after recrystallisation from benzene. The m. p. was not depressed by admixture with a specimen prepared from rubrene *iso*oxide by reduction with magnesium and methylmagnesium iodide according to Badoche (*loc. cit.*; see also Dufraisse and Badoche, *loc. cit.*, 1931). The specimen obtained by this method also had m. p. 175° unchanged by recrystallisation from benzene (lit., m. p. 177—178°).

5-*Phenoxy*-6 : 11 : 12-*triphenylnaphthacene.*—An intimate mixture of rubrene *iso*oxide (1·0 g.) and iron powder (10 g.) was refluxed with glacial acetic acid (150 c.c.) for 15 min., then poured into distilled water (750 c.c.). The solid was collected, washed until acid-free, air-dried, and extracted with benzene (Soxhlet) in the dark. After chromatography on alumina, the solution was concentrated, and the product collected and recrystallised from benzene–hexane. 5-*Phenoxy*-6 : 11 : 12-*triphenylnaphthacene* (0·3 g.) was obtained as short red laths, m. p. 325° (Found: C, 91·9; H, 5·2; O, 2·6. $C_{42}H_{28}O$ requires C, 91·9; H, 5·2; O, 2·9%). Unchanged *iso*oxide (0·4—0·5 g.) was also obtained from the chromatogram.

The m. p. of the phenoxytriphenylnaphthacene was not depressed on admixture with rubrene,

m. p. 325°. It was rapidly photo-oxidised but a homogeneous product could not be isolated. It was recovered unchanged after being shaken for 2 weeks in the dark with magnesium and methyl-magnesium iodide.

1 : 4 : 10-*Triphenyl*-2 : 3-*benzanthrone* (XVII).—(*a*) Rubrene *iso*oxide (1·0 g.) was dissolved in concentrated sulphuric acid (15 c.c.) at −10°, and set aside for 1 hr. The solution was poured on cracked ice, and the precipitated solid filtered off and washed until acid-free. The filtrate and washings were treated with bromine water, and the resulting 2 : 4 : 6-tribromophenol was collected (0·44 g., 75%) and identified by comparison with an authentic specimen. The initially precipitated solid was chromatographed on alumina. A small colourless band having a blue-violet fluorescence preceded the main yellow band. Elution of the former gave a few mg. of a pale yellow hydrocarbon, m. p. >400° (Found: C, 94·6; H, 5·6%). The absorption spectrum in chloroform had a maximum at 3180 Å (log ε 4·5). Elution of the main yellow band and recrystallisation from benzene–light petroleum gave **1 : 4 : 10-*triphenyl*-2 : 3-*benzanthrone*** (XVII) as yellow prisms, m. p. 244° (0·59 g.) (Found: C, 91·9; H, 5·3. $C_{36}H_{24}O$ requires C, 91·5; H, 5·1%).

(*b*) Rubrene *iso*oxide (40 mg.) was added slowly, with stirring, to just-molten potassium hydroxide (1·2 g.), in a nickel crucible. After cooling, the mixture was treated with water, and the solid collected and recrystallised from acetic acid. The triphenylbenzanthrone was obtained as yellow prisms, m. p. and mixed m. p. 244° (17 mg., 50%).

10-*Hydroxy*-1 : 4 : 10-*triphenyl*-2 : 3-*benzanthrone* (XV).—(*a*) A suspension of 6 : 11-diphenylnaphthacene-5 : 12-quinone (1·0 g.) in anhydrous benzene (60 c.c.) and 0·25M-phenylmagnesium bromide in ether (9·8 c.c.) was refluxed for 24 hr., then poured on ice and sulphuric acid. Further benzene was added to keep the solid in solution. The organic layer was dried (Na_2SO_4) and then chromatographed on alumina, benzene being used for development. A broad bright yellow band, which was eluted first, contained unchanged quinone. A second, pale yellow band, was held firmly on the upper half of the column. This was cut out and extracted with chloroform (Soxhlet). After evaporation to small volume and addition of a little hexane, the product separated. Recrystallisation from dry ether gave **10-*hydroxy*-1 : 4 : 10-*triphenyl*-2 : 3-*benzanthrone*** (XV) as pale yellow needles (0·3 g., 25%), m. p. 281—284° (decomp.) (Found: C, 88·8; H, 5·1; O, 6·6. $C_{36}H_{24}O_2$ requires C, 88·5; H, 4·9; O, 6·6%).

(*b*) A solution of 5-phenoxy-6 : 11 : 12-triphenylnaphthacene (0·5 g.) in boiling benzene (30 c c.) was treated with nitric acid (15%; 0·25 c.c.) during 30 min., by which time the colour and fluorescence had disappeared. The benzene solution was washed, dried, and evaporated. After recrystallisation from dry ether the hydroxytriphenylbenzanthrone was obtained as pale yellow needles, m. p. and mixed m. p. 282—283° (decomp.).

(*c*) A mechanically shaken solution of 5-phenoxy-6 : 11 : 12-triphenylnaphthacene (0·1 g.) in benzene (30 c.c.) was treated with cold 1% potassium permanganate (to which sulphuric acid, 0·5 c.c./l., had been added) a few c.c. at a time. The addition was stopped when the benzene layer had been decolorised. Sodium hydrogen sulphite solution was added to dissolve the manganese dioxide, and the benzene solution was then washed with water and dried (Na_2SO_4). After concentration and recrystallisation from ether, hydroxytriphenylbenzanthrone (80 mg., 90%) identical with that prepared as above was obtained.

Specimens made by all methods gave a characteristic grass-green colour with concentrated sulphuric acid in the cold. On heating, the colour changed to a reddish-brown. This type of colour reaction is given by many *meso*-hydroxyanthrones.

***Action of Filtered Phenylmagnesium Bromide on Rubrene* iso*Oxide*.**—(*a*) A solution of rubrene *iso*oxide (1 g.) in anhydrous benzene (30 c.c.) was added to filtered Grignard reagent prepared from bromobenzene (6·0 g.), magnesium turnings (0·9 g.) and ether (25 c.c.). The mixture was refluxed for 65 hr., the ether being allowed to escape in the first hour, and then poured on ice and sulphuric acid. The hydrolysate was steam-distilled, and the residue heated at 160—180°/0·01 mm. to remove diphenyl by sublimation. After further purification by chromatography and recrystallisation from ether–light petroleum, the product was obtained as red crystals (0·3 g.), m. p. 316° unchanged by further recrystallisation. It was identified as rubrene by analysis (Found: C, 94·3; H, 5·8. Calc. for $C_{42}H_{28}$: C, 94·7; H, 5·3%) and by its absorption spectrum. The m. p. was not depressed on admixture with rubrene.

In the purification of this product by chromatography, the fraction eluted from the column immediately after the red band yielded rubrene photo-oxide (90 mg.), identified by direct comparison with an authentic specimen. This product was evidently formed by photo-oxidation of the rubrene during the working up. Further elution of the column gave gums.

(*b*) A filtered ethereal solution of phenylmagnesium bromide (14 c.c.; 0·25M) was added to

rubrene *iso*oxide (1 g.) in benzene (30 c.c.), and the mixture refluxed for 24 hr., the ether being allowed to escape. After hydrolysis and steam-distillation as above, the product was chromatographed on alumina from benzene. Elution of the first band, followed by recrystallisation of the product from ethyl acetate, gave rubrene mono-oxide (0·18 g.), m. p. and mixed m. p. 320°. A little unchanged *iso*oxide was also isolated, but no other homogeneous material.

(*c*) A similar experiment was conducted but with 10·5 c.c. of the 0·25M-Grignard solution. Elution of the lowest band on the column gave no homogeneous material. A second yellow band was held firmly, and this was cut out and extracted with ether. Evaporation and recrystallisation of the product from ether gave 10-hydroxy-1 : 4 : 10-triphenyl-2 : 3-benzanthrone (78 mg.), m. p. and mixed m. p. 280° (decomp.), giving the characteristic colour reactions (see above).

trans-6 : 11-*Dihydro*-6 : 11-*dihydroxy*-5 : 6 : 11 : 12-*tetraphenylnaphthacene* (XVI).—Ethereal phenylmagnesium iodide (10 c.c.; 0·4M) and anhydrous benzene (60 c.c.) were boiled under reflux, hydroxytriphenylbenzanthrone (XV) (1·0 g.) being suspended in a Soxhlet thimble under the condenser. After 24 hr. the mixture was poured on ice and sulphuric acid, and the organic layer worked up in the usual way. Recrystallisation from ethyl acetate gave the colourless *trans*-diol (XVI), m. p. 251°, not depressed on admixture with a specimen prepared according to Dufraisse and Compagnon (*Compt. rend.*, 1938, **207**, 585; see also Allen and Bell, *J. Amer. Chem. Soc.*, 1940, **62**, 2408).

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The Phosphorescence Spectra of Naphthalene and Some Simple Derivatives.

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A photomultiplier technique has been used to measure the phosphorescence emission from naphthalene and some simple derivatives. The spectrum of naphthalene has been interpreted in terms of known vibration frequencies and an explanation advanced for the appearance of b_{1g} fundamentals. The reduction in the symmetry of the parent molecule brought about by simple substitution, causes marked changes in the spectrum, which are explained in some detail.

PREVIOUS methods of measuring the phosphorescence emission from naphthalene (Goldstein, *Phil. Mag.*, 1910, **20**, 619; Lewis and Kasha, *J. Amer. Chem. Soc.*, 1944, **66**, 2100; Terenin and Ermolaev, *Akad. Nauk S.S.S.R. Pamyati S.I. Vavilov*, 1952, 137) employed photography. Because of the low light intensity this necessitated low-dispersion instruments and rather large slit widths with resultant loss of accuracy.

Photoelectron multipliers have made possible the quantitative measurement of very low light intensities (cf. S. Rodda, " Photoelectric Multipliers," Macdonald, London, 1953) and opened a wide field particularly in molecular spectroscopy. We used a photoelectron multiplier with a constant-deviation glass spectrometer to measure quickly and accurately the emission from naphthalene and simple derivatives.

At the low temperatures (77° K) at which phosphorescence is usually studied the initial state may be taken as the zero-point vibrational level of the lowest triplet state. All frequency differences in the spectrum will then be characteristic of the ground state. Herzberg and Teller (*Z. physikal. Chem.*, 1933, *B*, **21**, 410) established the principles that govern the vibrational structure of an electronic transition. If the symmetry of the nuclei is unchanged by the transition the vibrations most strongly excited will be totally symmetric. Furthermore for an aromatic molecule these vibrations will be predominantly carbon (skeletal) motions.

Dikun and Sveshnikar (*Zhur. Eksper. Teoret. Fiz.*, 1949, **19**, 1000; *Doklady Akad. Nauk*

S.S.S.R., 1949, **65**, 637) and Shull (*J. Chem. Phys.*, 1949, **17**, 295) have shown that the phosphorescent level in benzene (identified with a triplet spin configuration by Lewis and Kasha, *loc. cit.*) is either $^3B_{1u}$ or $^3B_{2u}$ (point group D_{6h}) and the resulting transition to the ground (singlet) state is symmetry-forbidden. (References to symmetry apply here to spatial symmetry, the spin prohibition being understood.)

As quantum-mechanical calculations (Craig, *Proc. Int. Congr. Pure Appl. Chem.*, 1947, **11**, 411) predict the ground triplet of naphthalene to be $^3B_{2u}$, the transition to the ground state should be symmetry-allowed. This behaviour, in contrast to that observed with benzene, presents several interesting possibilities.

Naphthalene belongs to the point group D_{2h} and (cf. Kohlrausch and Seka, *Chem. Ber.*, 1938, *B*, **71**, 1551) possesses nine totally symmetric (a_g) vibrational modes, of which five are skeletal vibrations.

If the triplet–singlet transition is symmetry-allowed the vibrational pattern will be governed by the considerations outlined above. The spectrum should contain only five vibration frequencies, either singly or in progressions. Their relative intensities will depend on the change in size of the nuclear framework of the two states and the way in which the particular modes are able to incorporate this difference into their motion.

It is possible by simple substitution (simple, as used here, refers to single-atom substituents, so that the number of atoms in the molecule is unchanged) to reduce the point-group symmetry of the naphthalene molecule through C_{2h} to C_s. The new point groups have fewer symmetry requirements and a number of vibrations that were described by non-totally symmetric representations in naphthalene symmetry now fall into the totally symmetric representations of the lower point groups:

Species of D_{2h} (No. of skeletal vibrations)	Resolved into: Species of C_{2h}		Species of C_s
A_g (5), B_{1g} (4)	A_g (9)		A' (17)
B_{2g} (1), B_{3g} (2)	B_g (3)	A'' (7)	
A_u (2), B_{1u} (2)	A_u (4)		
B_{2u} (4), B_{3u} (4)	B_u (8)		A' (17)

This suggests that the vibrational pattern in passing from naphthalene to, say, a monohalogenonaphthalene might become quite complex, because the latter possesses 17 totally symmetric skeletal vibrations. These purely symmetry requirements, however, must be augmented by considerations of the dynamics of the vibrational motions. Only those vibrations whose dynamics satisfy the difference in framework size and shape will be strongly excited.

Results and Analysis.—The assignment column in the tables refers to known vibration frequencies (Luther, *Z. Elektrochem.*, 1948, **52**, 210, and Ferguson and Werner, to be published). The probable assignment column signifies that vibrational data are incomplete or lacking.

Naphthalene and 1 : 5-*dideuteronaphthalene.* See Figs. 1 and 2 and Table. The spectrum of naphthalene presents a marked contrast to that of benzene where the features are those of a forbidden transition. The major part of the intensity is carried off by progressions and combinations of only three frequencies, *viz.*, 512, 1380, and 1575 cm.$^{-1}$. The 1575 cm.$^{-1}$ vibration, however, is unexpected as it has been assigned to a b_{1g} motion (Pimentel and McClellan, quoted by Barrow and McClellan, *J. Amer. Chem. Soc.*, 1951, **73**, 573; Luther, *loc. cit.*). The other two are well-known a_g skeletal vibrations observed in the fluorescence spectrum of naphthalene. It should also be noted that another b_{1g} mode plays a part, *viz.*, the 1146 cm.$^{-1}$, although to a much lesser extent than the others (see Fig. 1 and Table). As these assignments are too well established to be seriously doubted, the explanation must come from a change of equilibrium configuration symmetry between the lowest triplet and singlet states.

Band position, cm.$^{-1}$	Separation from 0,0	Assignment	Band position, cm.$^{-1}$	Separation from 0,0	Assignment	Band position, cm.$^{-1}$	Separation from 0,0	Assignment
				Naphthalene				
21,246	—	0,0	19,856	1390	1380,0	18,820	2426	2 × 512 +
20,730	516	512,0	19,665	1581	1575,0			+ 1380,0
20,200	1046	2 × 512,0	19,355	1891	512 + 1380,0	18,440	2806	2 × 1380,0
20,105	1141	1146,0	19,200	2046	512 + 1576,0	18,269	2987	1380 + 1576,0
				1 : 5-*Dideuteronaphthalene*				
21,260	—	0,0	19,719	1541	1541,0	18,590	2670	1112 + 1541,0
20,760	500	500,0	19,390	1870	500 + 1386,0	18,480	2780	2 × 1386,0
20,148	1112	1112,0	19,185	2075	500 + 1541,0	18,315	2945	1386 + 1541,0
19,874	1386	1386,0	18,800	2460	1112 + 1380,0	18,700	3090	2 × 1541,0
				α-*Fluoronaphthalene*				
21,062	—	0,0	19,474	1588	1576,0	18,500	2562	1153 + 1378,0
20,830	230	224,0	19,190	1872	526 + 1378,0	18,280	2782	2 × 1378,0
20,554	508	526,0	18,930	2132	526 + 1576,0	18,110	2952	1378 + 1576,0
19,900	1162	1153,0	18,730	2332	2 × 1153,0	17,890	3172	2 × 1576,0
19,684	1378	1378,0						
				β-*Fluoronaphthalene*				
21,268	—	0,0	19,878	1390	1390,0	18,730	2538	1173 + 1390,0
20,804	464	464,0	19,682	1586	1586,0	18,500	2768	2 × 1930,0
20,500	768	768,0	19,425	1843	464 + 1390,0	18,285	2983	1390 + 1586,0
20,340	948	948,0	19,215	2053	464 + 1586,0	18,080	3188	2 × 1586,0
20,095	1173	1173,0						
				α-*Chloronaphthalene*				
20,645	—	0,0	19,269	1376	1368,0	18,350	2295	2 × 1159,0
20,440	205	222,0	19,118	1527	1565,0	18,145	2500	1159 + 1380,0
20,125	520	515,0	18,760	1885	515 + 1368,0	17,930	2715	2 × 1380,0
19,710	935	954,0	18,585	2060	515 + 1565,0	17,725	2920	1368 + 1565,0
19,480	1165	1159,0						
				β-*Chloronaphthalene*				
21,069	—	0,0	19,674	1395	1386,0	18,845	2224	1386 + 863,0
20,784	285	281,0	19,430	1639	1624,0	18,260	2809	1624 + 1153,0
20,558	511	516,0	19,182	1887	1386 + 516,0	18,030	3039	1624 + 1386,0
20,232	837	863,0	18,930	2139	1624 + 516,0	17,830	3239	2 × 1624,0
				α-*Bromonaphthalene*				
20,652	—	0,0	19,610	1042	1055,0	18,530	2122	1363 + 731,0
20,495	157	176,0	19,300	1352	1363,0	18,340	2312	1559 + 731,0
20,330	322	304,0	19,116	1536	1559,0	17,945	2706	2 × 1363,0
20,138	514	511,0	18,740	1912	1363 + 511,0	17,740	2912	1559 + 1363,0
19,892	740	731,0						
				β-*Bromonaphthalene*				
21,036	—	0,0	19,648	1388	1376,0	19,182	1854	1574 + 276,0
20,782	254	276,0	19,452	1584	1574,0	18,810	2226	1376 + 812,0
20,528	508	519,0	19,390	1646	1376 + 276,0	18,650	2386	1574 + 812,0
20,218	818	812,0						
				1 : 5-*Dibromonaphthalene*				
20,086	—	0,0	18,960	1126	1126,0	18,010	2076	1536 + 494,0
19,592	494	494,0	18,720	1366	1366,0	17,780	2306	1536 + 758,0
19,328	758	758,0	18,550	1536	1536,0	17,300	2786	2 × 1366,0
19,140	946	946,0	18,240	1846	1366 + 494,0			
				2 : 6-*Dibromonaphthalene*				
20,806	—	0,0	19,740	1066	1066,0	18,665	2141	1360 + 796,0
20,560	246	246,0	19,446	1360	1360,0	18,415	2391	1538 + 796,0
20,302	504	504,0	19,268	1538	1538,0	18,080	2726	2 × 1360,0
20,010	796	796,0	18,920	1886	1360 + 504,0	17,885	2921	1538 + 1360,0
19,820	986	986,0	18,730	2076	1538 + 504,0	17,690	3116	2 × 1538,0

This change of symmetry can come about in either or both of two ways. The triplet state may be inherently distorted or else the presence of the solvent introduces a perturbation sufficiently strong to distort one of the states slightly more than the other. To test these explanations we used 1 : 5-dideuteronaphthalene which has the point-group symmetry C_{2h} in the ground state, and in which the four skeletal b_{1g} vibrations of naphthalene become totally symmetric in the new point group (see Table). The substitution of deuterium for

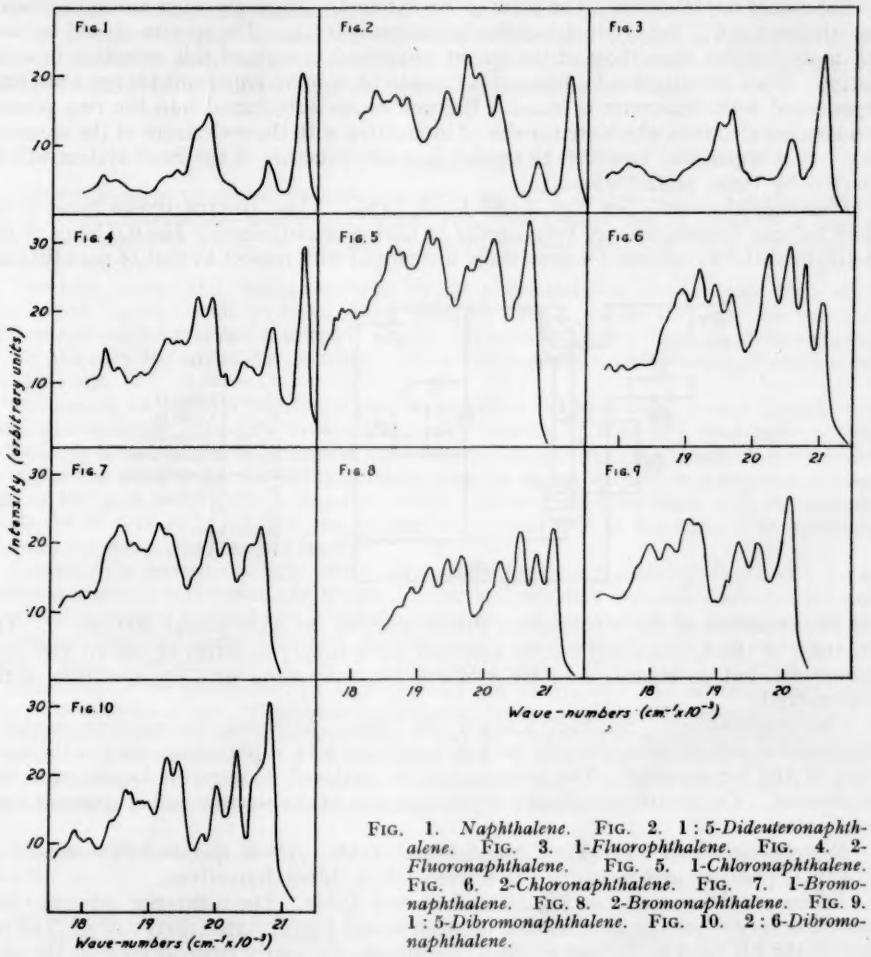

FIG. 1. *Naphthalene.* FIG. 2. 1 : 5-*Dideuteronaphthalene.* FIG. 3. 1-*Fluorophthalene.* FIG. 4. 2-*Fluoronaphthalene.* FIG. 5. 1-*Chloronaphthalene.* FIG. 6. 2-*Chloronaphthalene.* FIG. 7. 1-*Bromonaphthalene.* FIG. 8. 2-*Bromonaphthalene.* FIG. 9. 1 : 5-*Dibromonaphthalene.* FIG. 10. 2 : 6-*Dibromonaphthalene.*

hydrogen will not significantly alter the configuration of the carbon framework, so that comparison of its phosphorescence with that of naphthalene should show how b_{1g} fundamentals become active in the naphthalene spectrum.

As can be seen from Fig. 2, the contribution to the intensity distribution made by the 1575 and 1146 cm.$^{-1}$ b_{1g} modes of naphthalene increases greatly relative to that of the naphthalene a_g fundamentals. This then points to the distortion of the molecule by solvent perturbations as the explanation for the appearance of b_{1g} fundamentals in naphthalene.

The appearance of b_{1g} fundamentals by perturbation of an appropriate electronic state was considered improbable in view of the large increase of their intensity in the dideutero-

compound. If they were stealing intensity from another level then substitution by deuterium would not affect it to the degree observed. The 1575 cm.$^{-1}$ fundamental, from observation with the substituted naphthalenes, is particularly suitable for excitation in this transition and it seems likely that even a small perturbation of the molecule enables it to appear.

The height of the peak representing one quantum of the 512 cm.$^{-1}$ a_g vibration of naphthalene bears the same ratio to that of the 0,0 band for both compounds.

Substituted naphthalenes. The point-group symmetry for single-atom monosubstituted naphthalenes is C_s; for symmetrical disubstitution it is C_{2h}. The spectra should be, and are, more complex than those of the parent compound because of this reduction in symmetry. When substitution by halogen is considered, a more important change than that experienced with deuterium is found. Halogen atoms substituted into the ring possess non-bonding electrons which are capable of interacting with the π-electrons of the aromatic ring. It is impossible, however, to predict how the structure of the band system will be affected by these perturbations.

Fluoronaphthalenes. See Figs. 3 and 4 and Table. These spectra, unlike those of the other halogen derivatives, are very similar to that of naphthalene. The 0,0 band of the spectrum of the β-compound is practically unchanged with respect to that of naphthalene,

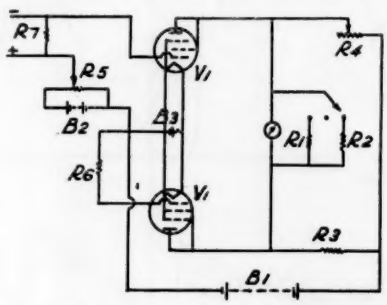

FIG. 11.
$R_1 = 10\ \Omega$.
$R_2 = 170\ \Omega$.
$R_3 = 15{,}000\ \Omega$.
$R_4 = 17{,}000\ \Omega$.
$R_5 = 1$ megohm.
$R_6 = 10$ megohm.
$R_7 = 130$ megohm.
$B_1 = 67\frac{1}{2}$ v.
$B_2 = 7\frac{1}{2}$ v.
$B_3 = 1\frac{1}{2}$ v.
$V_1 = 1T4$.

but the spectrum of the α-compound suffers a slight red shift (about 200 cm.$^{-1}$). The spectrum of the α-compound can be analysed quite simply in terms of known vibration frequencies, but no Raman data are available for comparison with the spectrum of the β-compound.

Chloronaphthalenes. See Figs. 5 and 6 and Table. As before, the spectrum of the α-compound is shifted more towards the red, compared with naphthalene, than is the spectrum of the β-compound. The systems can be analysed in terms of known vibration frequencies. The greater complexity of the spectrum of the α-compound is apparent from the Figures.

Bromonaphthalenes. See Figs. 7 and 8 and Table. These spectra follow closely in structure, position, and intensity the corresponding chloro-derivatives.

Dibromonaphthalenes. See Figs. 9 and 10 and Table. The difference between these spectra is very much the same as that between α- and β-substituted derivatives. The red shift of the 0,0 band in the case of the 2 : 6-compound is nearly twice as great as the shift for the β-mono-derivative and is much less than the shift for the 1 : 5-compound, which again is nearly twice as great as the shift for the α-mono-derivative.

As in the monochloro- and -bromo-derivatives a low vibration becomes quite prominent in the spectrum of the 2 : 6-derivative. Although this vibration does not appear in the spectrum of the 1 : 5-derivative, the asymmetry of the first band suggests that it might be concealed under it.

No Raman data are available to verify assignments.

Conclusions.—The phosphorescence emission of naphthalene is unique in that its vibrational pattern is strongly dependent on the point-group symmetry of the molecule. Although naphthalene possesses 48 different vibrational modes, the requirements enforced

by symmetry and the nature of the electronic states involved in the transition are such that the spectrum is extremely simple and can be interpreted in terms of a few characteristic frequencies. These frequencies still predominate in the spectra of the substituted naphthalenes, but the appearance of new vibrations, particularly low-frequency modes, makes their pattern quite complex, although still interpretable with known vibration frequencies.

The 1575 cm.$^{-1}$ b_{1g} mode of naphthalene, probably because of its mechanics, is particularly suitable for excitation in the spectrum and it appears even in the naphthalene spectrum because of solvent perturbations.

The phosphorescence emission of naphthalene therefore records a characteristically allowed transition from the ground-triplet to the ground-singlet state. From theoretical calculations this level probably has the symmetry classification $^3B_{2u}$.

Experimental

Apparatus.—The photoelectron multiplier used was a R.C.A. type 1P21. The spectrograph was a Hilger, glass-prism, constant-deviation type, with a dispersion of about 20 Å/mm. at 4350 Å and about 60 Å/mm. at 5790 Å. The multiplier was fixed and the prism rotated to record the spectrum.

The high, stable, D.C. voltage required by the photomultiplier was provided by a slight adaption of Zimm's circuit (*J. Chem. Phys.*, 1948, **16**, 1102). As the D.C. amplifier was very efficient and stable the circuit is shown in Fig. 11. It includes a low-voltage supply to compensate for the dark current of the phototube. This had to be balanced before each reading but changed little.

Calibration for spectral sensitivity was made with a tungsten lamp standardized by the National Standards Laboratory, Sydney. By use of Planck's equation for a black-body radiator and making allowance for the change in dispersion of the spectrograph, correction factors were determined so that the curves finally obtained give the energy emitted as a function of wave number for equal band width in Ångström units. All readings were taken with the spectrograph slit at 0·14 mm. and the slit before the photocathode at 0·2 mm. The estimated accuracy for sharp peaks is $\pm$15 cm.$^{-1}$.

Solvent.—The solvent was light petroleum, purified by being repeatedly stirred with a concentrated sulphuric acid–oleum mixture until no further coloration occurred, washed, dried, and distilled, the fraction boiling at 58—60° being collected. It freezes easily to a clear, rigid, glass without cracking and keeps free from phosphorescent impurities even on long storage. We found it much more convenient to use than the more generally known E.P.A. mixture.

Compounds.—We thank Miss B. J. Russell for the sample of 1 : 5-dideuteronaphthalene, which was analysed as 94% of dideuteronaphthlaene and 6% of monodeuteronaphthalene. For the dibromo-compounds we thank Miss Russell and Mr. Hunt. The physical constants are as follows: m. p. naphthalene, 80°, 1 : 5-dideutero-, 79·8°, β-fluoro-, 60°, β-chloro-, 62°, β-bromo-, 59°, 1 : 5-dibromo-, 129°, and 2 : 6-dibromo-naphthalene, 160°. B. p. α-fluoro-, 48°/0·6 mm., α-chloro-, 73°/0·2 mm., and α-bromo-naphthalene, 101°/1·5 mm.

We thank Professor D. P. Craig for his interest and help and for many stimulating discussions.

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A Prediction of the Reactivity of Some Penta- and Hexa-cyclic Hydrocarbons.

By P. H. Gore.

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Dewar's simplified M.O. treatment has been applied to more complex polycyclic hydrocarbons, *viz.*, anthanthrene, the five dibenzophenanthrenes, the five dibenzopyrenes, and zethrene. Results obtained have been correlated with the geometry of the systems. Some recorded experimental results are discussed, including the abnormal acidity of 1 : 2-6 : 7-dibenzopyren-3-ol and the structure of the cation formed by zethrene in acid media.

The simplified molecular-orbital method devised by Dewar (*J. Amer. Chem. Soc.*, 1952, **74**, 3357; *Ann. Reports*, 1951, **48**, 116; "Progress in Organic Chemistry," ed. Cook, Butterworths Scientific Publ., London, 1953, Vol. II, p. 1) for the evaluation of the reactivity of the substituent positions of even alternant hydrocarbons has given results in excellent general agreement with experiment. The present contribution is an extension of the method to some higher ring systems.

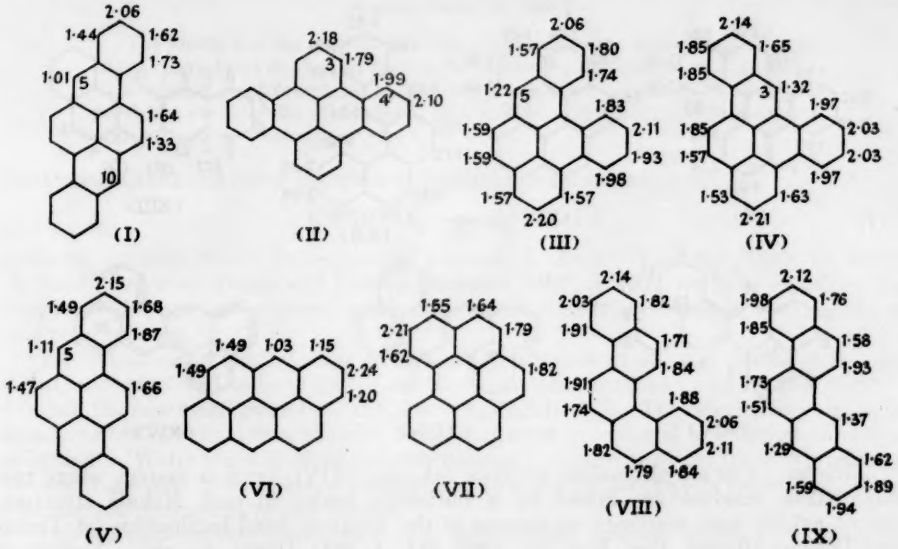
3 : 4-8 : 9-Dibenzopyrene (I) is substituted readily in the 5- and the 5 : 10-positions (Ioffe and Efros, *J. Gen. Chem., U.S.S.R.*, 1946, **16**, 111). ΔE_π values * were accordingly determined by Dewar's (*loc. cit.*) procedure; the lowest value was found for the 5-position, in agreement with experiment. Further, the observed value of ΔE_π (1·01β) is lower than for any other hydrocarbon previously investigated (except pentacene), and the dibenzopyrene (I) should therefore be very reactive. This hydrocarbon is further of interest because of its carcinogenic properties (Kleinenberg, *Arch. Sci. biol., U.R.S.S.*, 1938, **51**, No. 3, 127; 1939, **56**, No. 3, **39**; Tretyakova, *Bull. Biol. Med. Exp. U.R.S.S.*, 1941, **11**, 496; *Chem. Abs.*, 1947, **41**, 6621).

Evidence concerning the "reactivity" of 1 : 2-6 : 7-dibenzopyrene (II) is indirect: Clar (*Ber.*, 1943, **76**, 609) showed that the acidity of its 3-hydroxy-derivative is abnormally low for a polycyclic phenol. ΔE_π values of the various positions of (II) were therefore obtained: as can be seen, the 3-position should be most readily substituted. Normally a tendency for substitution at a given position is related to the extent of conjugation between the ring system and a substituent group in that position. It follows that the 3-phenol of (II) ought to have the highest acid strength, comparable with that of α-naphthol. The abnormal acidity must be connected with the sterically hindered nature of this position. The large hydroxyl group will almost certainly be displaced out of the plane of the rings by steric interference with the hydrogen atom in the 4'-position and this (cf. Dewar, *loc. cit.*; Brown, *J.*, 1952, 2231; Guy, *J. Chim. phys.*, 1949, **46**, 469) would lower the conjugative interaction between the p-electrons of the hydroxyl-oxygen atom and the π-electron system of the polycyclic hydrocarbon residue. In this manner the low acidity of 3-hydroxy-1 : 2-6 : 7-dibenzopyrene is accounted for, as well as the surprisingly similar absorption spectrum of the phenol and the parent hydrocarbon (Clar, *loc. cit.*). In a like manner, other sterically hindered derivatives of polycyclic hydrocarbons may be predicted to behave abnormally: *e.g.*, the 4-derivatives of phenanthrene and the 1-derivatives of triphenylene should show a low acidity of the hydroxy- and carboxy-derivatives, and a high basic strength for the amines. Steric hindrance can be appreciable in the 1-triphenylene position, as Rapson (*J.*, 1941, 15) showed that 1-methoxytriphenylene resisted demethylation. However, it is possible, in these simpler cases, that conjugation occurs to an appreciable extent, with buckling of the ring system (as in the related cases of "intramolecular overcrowding;" cf. Newman *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 978, 3023; 1948, **70**, 1913; 1949, **71**, 3664; 1952, **74**, 3225; Bell and Waring, *J.*, 1949, 2689; Badger, Campbell, Cook, Raphael, and Scott, *J.*, 1950, 2326; Hernik, Herbstein, and Schmidt,

* ΔE_π = π-electron localisation energy (in terms of β) at the point of attack = $2\beta(a_1 + a_2) = 2\beta S$, where a_1 and a_2 are the NBMO coefficients of the transition state (as visualised by Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900) at the carbon atoms next to the one substituted (cf. Dewar, *locc. cit.*).

Nature, 1951, **168**, 158), in which case the 3-hydroxydibenzopyrene would be abnormal owing to the greater rigidity of the ring system (II).

The data for the isomeric dibenzopyrenes are given in (III—V), and those for the related anthanthrene in (VI). The study of 1 : 12-benzoperylene (VII) appeared relevant on account of the formation of alkyl derivatives of unknown orientation from zinc dust



fusion of erythroaphin-*sl* (Brown, Johnson, Quayle, and Todd, *J.*, 1954, 107). Certain pentacyclic hydrocarbons which were not investigated by Dewar, *viz.*, (VIII—XII), are also included. Not only were theoretical data available for only one of these known substances,* but they would prove of value in testing a proposed correlation between predicted reactivity and the geometry of polycyclic hydrocarbons. Such a correlation can now be stated : the reactivity of even complex systems can be predicted qualitatively by reference to simpler component structures.

Thus, in anthanthrene and each of the dibenzopyrenes the most reactive carbon atom corresponds to the *meso*-position in anthracene. For the derivatives of pyrene, this position corresponds also to one of the four most reactive positions of pyrene itself (in which these are equivalent). In this fashion the susceptibility to substitution of a position may be regarded as an additive property of component structures.

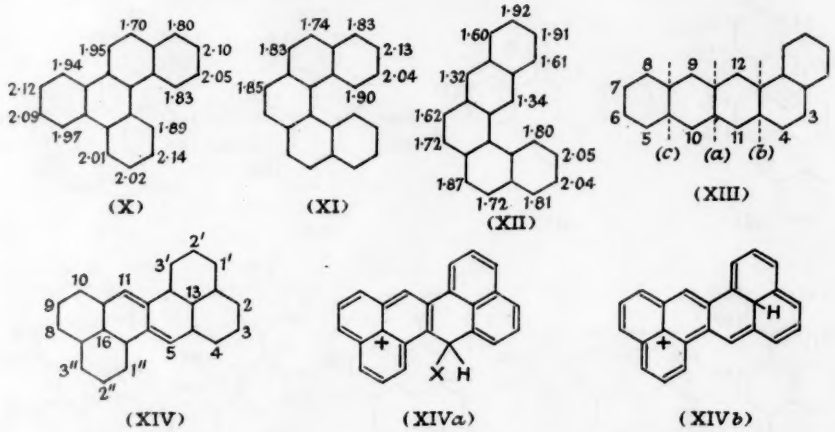
By angular superposition of two naphthalene structures the reactivity of the phenanthrene positions can be gauged : 9- (one α plus one β), 1- and 4- (one α), and 2- and 3- (one β), which is roughly the sequence of ΔE_π values quoted by Dewar (*loc. cit.*).

According to Dewar's ΔE_π values, the most reactive component hydrocarbon of 1 : 2-benzonaphthacene is naphthacene; this has four equivalent very reactive *meso*-positions, which in this benzo-derivative are different. To determine which of these will be the most reactive, the structure is separated into two components, either a naphthalene and a phenanthrene (division at *a* in XIII), or into an anthracene and a naphthalene unit (*b*) : in both cases the 9- and the 10-position are the most reactive. Choice between these two is obtained by consideration of a third component system, benzene and 1 : 2-benzanthracene (*c*). By using the analogy with 1 : 2-benzanthracene it will be concluded that

* 1 : 2-3 : 4-Dibenzophenanthrene (X) was examined by Buu-Hoï, Daudel, and Vroelant (*Bull. Soc. chim.*, 1949, 211) by the method of molecular diagrams, and reactivity predicted in the sequence $8>5 = 1' = 4' = 1'' = 4''>9>10>6 = 7 = 2' = 3' = 2'' = 3''$, these differing appreciably from our results. This hydrocarbon is of interest on account of its carcinogenic nature (Harris and Bradsher, *Cancer Res.*, 1946, **6**, 671).

ΔE_π values of the positions of 1 : 2-benzonaphthacene should increase in the sequence $10 < 9 < 11 < 12$, etc., as found by Dewar (*loc. cit.*).

This method of geometrical analysis of investigating "reactivity" has been applied to all the hydrocarbons mentioned in this paper, and those given by Dewar (*loc. cit.*), and only a verv few exceptions were noted.



Zethrene.—Clar's hydrocarbon zethrene (*op. cit.*) (XIV), being a system where two naphthalene residues are linked by a butadiene bridge in each Kekulé structure, should exhibit high reactivity on account of the apparent bond localisation (cf. Dewar and Longuet-Higgins, *Proc. Roy. Soc.*, 1952, **214**, *A*, 482; Dewar, *loc. cit.*). Analysis of zethrene by Dewar's procedure proved of interest. ΔE_π values for the 3′- (1·02β), 1′- (0·95β), 2- (0·86β), and 4-position (0·88β) were obtained in a normal fashion, the 2′- and the 3-position (2·12β) behaving like isolated β-naphthyl positions, whilst the 5-position, though abnormal in that $C_{(16)}$ becomes inactive with complete isolation of one naphthalene unit, gave $\Delta E_\pi = 0{\cdot}81\beta$, pointing to very high reactivity of the order of the *meso*-position in pentacene ($\Delta E_\pi = 0{\cdot}80\beta$, Dewar, *loc. cit.*). Coulson and Moser (*J.*, 1953, 1341) in a detailed M.O. investigation obtained the same sequence for free valences in the ground state of zethrene, pointing to the same sequence of reactivity in radical reactions. Here too (free valence for the 5-position = 0·210) the reactivity is to be expected to be appreciably higher than for, say, anthracene (free valence for the *meso*-position = 0·202; Burkitt, Coulson, and Longuet-Higgins, *Trans. Faraday Soc.*, 1951, **47**, 553). In an electrophilic substitution of zethrene by means of a reagent X^+, the transition state (XIV*a*) (Wheland, *loc. cit.*; cf. Dewar, *loc. cit.*), involving entry of the group at the 5-position, is resonance-stabilised, the formal charge being able to be written on seven carbon atoms.

In acid solution (XIV*a*; X = H) might be formed in this manner, and this could account for the formation of the "zethrenium" cation under acidic conditions (Clar, *op. cit.*, p. 95). This would require the hydrogen ion to be an electrophilic reagent, a behaviour which is now well established (Ingold, Raisin, and Wilson, *Nature*, 1934, **134**, 734; *J.*, 1936, 915, 1637; Gold and Long, *J. Amer. Chem. Soc.*, 1953, **75**, 4543). The present case differs from the examples of isotopic hydrogen exchange cited in that the transition state is apparently much more stable than usual, and elimination of a proton is not favoured. In Clar's alternate formulation of this cation (XIV*b*) (*op. cit.*), both naphthalene systems become degenerate and the hydrogen becomes attached to the somewhat hindered 13-position. In the absence of published experimental data, structure (XIV*a*) is therefore considered more likely for the "zethrenium" cation.

The author thanks Professor M. J. S. Dewar for helpful comments.

Acton Technical College, London, W.3. [*Received, March 27th*, 1954.]

Organosilicon Compounds. Part IX. The Reaction between Iodine and Trisubstituted Silanes.*

By D. R. Deans and C. Eaborn.

[Reprint Order No. 5261.]

The kinetics of the reaction between iodine and some trialkyl- and triarylsilanes have been studied in carbon tetrachloride, chloroform, and benzene. The reaction is of fourth order, and the mechanism proposed involves predominant electrophilic attack by I_4 on hydrogen and a less important nucleophilic attack (or " solvation ") by I_2 on silicon.

Trialkylsilanes and iodine in carbon tetrachloride react according to :

$$R_3SiH + I_2 \longrightarrow R_3SiI + HI \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

(Eaborn, *J.*, 1949, 2755; Nebergall and Johnson, *J. Amer. Chem. Soc.*, 1949, **72**, 4022). As briefly reported (Deans and Eaborn, *Research*, 1952, **5**, 592), we have examined the kinetics of this process for several trialkylsilanes and some triarylsilanes in weakly polar or non-polar solvents.

The iodination of triethylsilane in carbon tetrachloride at 25° was examined in most detail, and was found to be of fourth order over the concentration range studied (0·033—0·005M), the rate being given by $-d[I_2]/dt = k_4[Et_3SiH][I_2]^3$. The reaction appears to be homogeneous and chain-free, the rate being unaffected by removal or addition of oxygen or by light. Water has little effect (possibly because it is taken up by the reaction products), but small amounts of α-picoline or ethanol lead to rapid but incomplete removal of iodine. The reaction products have no influence.

The fourth-order rate constants remain satisfactorily constant within a run over the temperature range 25° to −16°, and the temperature coefficient is small and variable, as is common in high-order reactions, and there may be an inversion of the temperature coefficient below 0°, as shown by the following figures :

Temp.	−18·5°	−16·0°	−9·2°	1·1°	9·7°	25°
$10^{-3}k_4$ (mole^{-3} l.^{3} hr.$^{-1}$)	4·6	4·9	4·3	4·9	6·4	11·3

At 55°, however, the order within a run is between third and fourth, suggesting that a lower-order reaction, obscured at lower temperatures, has become more prominent, as in high-order aromatic halogenation and addition of halogens to olefins (Robertson and co-workers, *J.*, 1937 onwards).

Variation in Silane and Solvent.—The rates of iodination of various silanes in three solvents are shown in the following table. Satisfactory kinetics were not obtained for all

$10^{-3} \times$ *Fourth-order rate constants* (*mole*$^{-3}$ *l.*^{3} *hr.*$^{-1}$) *at* 25°.

Silane	CCl_4	C_6H_6	$CHCl_3$	Silane	CCl_4	C_6H_6	$CHCl_3$
Tri-*p*-chlorophenyl-	—[a]	—[a]	0·4	Tri*iso*propyl	—	14·5	—
Triphenyl-	0·1	—[b]	22	Tri-*n*-propyl-	10·9	63·6	—
Tri-*p*-tolyl-	0·5	—	—[c]	Triethyl-	11·3	278	2120
Tri*iso*butyl-	1·4	3·4	—	Tri-*n*-butyl-	18·0	75·3	5960

[a] Too slow to be followed accurately. [b] Acid-titre low throughout. [c] Fast, but iodine returns to solution.

the compounds in all the solvents mainly because of decomposition of the products, and for the trialkylsilanes a rate constant is given only if it remained satisfactorily constant through a run. The figures for the triarylsilanes are less reliable than those for the trialkylsilanes, but for a triarylsilane listing of a rate constant means that it remained reasonably constant throughout a run when the first 10% of reaction was neglected (a faster initial reaction may in these cases be due to traces of water, and is being investigated). However,

* Part VIII, *J.*, 1954, 939.

it is clear that the reactivity decreases in the order tri-*p*-tolyl-, triphenyl-, tri-*p*-chlorophenyl-silane, so that the reaction is facilitated by electron-release towards silicon. This is confirmed by the absence of detectable interaction of trichlorosilane (having three electronegative atoms attached to the silicon) with iodine in chloroform, or with iodine, and even bromine, in carbon tetrachloride at 25°.

In benzene the order of reactivity of the trialkylsilanes, R_3SiH, is (R =) Et>Bu^n>Pr^n>Pr^i>Bu^i and there must be some steric hindrance, since otherwise the stronger electron-release of the *iso*propyl group would lead to a greater reactivity for tri*iso*propylsilane. However, the tri*iso*propylsilicon system has not the characteristic markedly low reactivity it shows in reactions involving predominant nucleophilic attack on silicon (cf. Eaborn, *J.*, 1952, 2840; 1953, 494; and refs.) since tri*iso*propylsilane reacts at one-fifth of the rate of the tri-*n*-propyl compound and is actually more reactive than tri*iso*butylsilane. The order of reactivity of the trialkylsilanes probably results from counteracting polar and (small) steric factors.

The reaction rate increases with polarity of the solvent, in the order: carbon tetrachloride, benzene, chloroform. In agreement with this, iodine reacts rapidly with trialkylsilanes in nitrobenzene or dioxan, but it then returns to the solution as the reaction products decompose.

Mechanism of the Reaction.—The usual difficulties with high-order reactions preclude certainty that the reaction is exactly of fourth order and not of mixed order approximating to four. Third-order processes particularly may be playing an undetected part. The generality of the agreement with the fourth-order equation for several compounds at several concentrations and temperatures, and in three solvents, suggests that the iodination is really of fourth order. The main conclusion below, that attack is predominantly electrophilic on hydrogen, would not be affected by changing the number of iodine molecules present in the transition state.

Heterolytic fission of the Si–H bond seems always to occur in the sense Si^+H^-, as expected from relative electronegativities. The absence of a large steric factor indicates strongly that the reaction does not go exclusively by nucleophilic attack on silicon (and it should be noted that iodide ion does not attack trialkylsilanes even in aqueous ethanol which would assist separation of hydride ion) and the following rate-determining transition states must be considered. (A cyclic transition state, combining the features of all three, is sterically improbable, and would require little effect of solvent on the rate.)

$$R_3\overset{\delta+}{Si}\ldots H\ldots I\ldots \overset{\delta-}{I_5} \qquad (a)$$

$$\overset{\delta+}{I_3}\ldots I\ldots \overset{R_3}{Si}\ldots H\ldots I\ldots \overset{\delta-}{I} \qquad (b)$$

$$\overset{\delta+}{I}\ldots I\ldots \overset{R_3}{Si}\ldots H\ldots I\ldots \overset{\delta-}{I_3} \qquad (c)$$

Transition state (*a*) seems unlikely since tri*iso*propylsilane should then be more reactive than triethylsilane, and furthermore it is difficult to see why an I_6 complex should be so much more effective an electrophilic agent than an I_4 complex, particularly since the latter should be present in much greater concentration; (*b*) seems improbable in that it would lead to I^- and I_3^+ ions, whereas (*c*) would lead to the more likely I^+ and I_3^- ions. If transition state (*c*) is accepted, the order of three with respect to iodine is understandable, for one molecule is needed to attack silicon, while as an electrophilic agent the more polarizable I_4 is more powerful than I_2. Since electron-supply to silicon facilitates reaction, the electrophilic attack on hydrogen must be more important in the transition state than the nucleophilic attack on silicon. Absence of catalysis by hydrogen iodide confirms that little driving force is coming from nucleophilic attack. Indeed, the I_2 entity in the transition state could be regarded as " solvating " the forming siliconium ion rather than being attached by a partial covalent bond, its function being to stabilise the forming siliconium ion by dispersing the positive charge. If this is so, lower reaction orders would be expected in more powerfully solvating media. (The high and variable orders found in weakly polar

solvents in halogenation of aromatics and addition of halogen to olefins could similarly be attributed to participation of one or more iodine molecules in " solvation " of a forming carbonium ion.)

There are several routes by which the transition state could be reached, involving various intermediate complexes; a reasonable scheme would be :

$$I_2 + I_2 \overset{\text{fast}}{\rightleftharpoons} I_4;\ R_3SiH + I_4 \overset{\text{fast}}{\rightleftharpoons} R_3SiH,I_4;\qquad I_2 + R_3SiH,I_4 \overset{\text{slow}}{\longrightarrow} R_3SiI + HI + 2I_2$$

The complex R_3SiH,I_4 is formally analogous to the R_3SiI,I_2 complex (Eaborn, *J.*, 1953, 4154), the more polarisable I_4 being required to form a complex with the less polar Si–H bond.

The conclusion that the main attack is electrophilic on hydrogen is in accord with the fact that electron-release to silicon facilitates this reaction and hinders the alkaline hydrolysis of organosilanes, in which nucleophilic attack on silicon predominates (Gilman and Dunn, *J. Amer. Chem. Soc.*, 1951, **73**, 3404; Gilman, Dunn, and Hammond, *ibid.*, p. 4499; Kaplan and Wilzback, *ibid.*, 1952, **74**, 6152; Price, *ibid.*, 1947, **69**, 2600). As expected, the latter reaction is also subject to large steric hindrance (Gilman and Brannen, *ibid.*, 1951, **73**, 4640). Because of d_π–p_π bonding between a silicon atom and an aromatic ring it is difficult to predict whether the triphenylsilyl group should release electrons more or less readily than trialkylsilyl, but the lower reactivity of triarylsilanes in iodination is in harmony with their higher reactivity in alkaline hydrolysis (Gilman and Dunn, *loc. cit.*).

Other Halogens.—Triethylsilane was found to react very rapidly with iodine monochloride in carbon tetrachloride according to $2Et_3SiH + 2ICl \longrightarrow 2Et_3SiCl + I_2 + 2HCl$. The reaction could go through either of the sequences,

$$Et_3SiH + ICl \longrightarrow Et_3SiI + HCl;\qquad Et_3SiI + ICl \longrightarrow Et_3SiCl + I_2$$

or

$$Et_3SiH + ICl \longrightarrow Et_3SiCl + HI;\qquad HI + ICl \longrightarrow HCl + I_2$$

since both hydrogen iodide and triethyliodosilane react rapidly with iodine monochloride to liberate iodine; the second sequence is more probable in view of the directions of polarisation of Si–H and I–Cl bonds.

Bromine in carbon tetrachloride reacts much more readily than iodine with trisubstituted silanes, and, contrary to a recent assertion (Gilman and Dunn, *Chem. Reviews*, 1953, **52**, 92), it reacts rapidly even with triphenylsilane, but the reaction does not go to completion, possibly because of the formation of unreactive complexes between bromine and the products.

Experimental

Materials.—Trialkylsilanes were fractionated in a column (12 theoretical plates) packed with glass helices. Triarylsilanes were recrystallized to constant m. p.

" AnalaR " carbon tetrachloride and chloroform were dried over and distilled from fresh phosphoric oxide. Benzene was dried over calcium hydride and distilled from phosphoric oxide.

Reaction Products.—Trialkyliodosilanes were obtained in good yield from interaction of triethyl-, tri-*n*-propyl-, and tri-*n*-butyl-silane and iodine in carbon tetrachloride. Isolation of tri*iso*butyl-, tri*iso*propyl-, and triaryl-iodosilanes was not attempted. Only when the iodine removed and acid produced (including that from hydrolysis of silicon iodides) agreed with eqn. (1) have the results been used.

With triethylsilane in carbon tetrachloride the course of the reaction was shown rigorously to conform with eqn. (1) by determination, at intervals, not only of iodine and acid but also of triethylsilane remaining (by measuring hydrogen evolved when a sample of the reaction mixture was added to excess of ethanolic alkali).

Kinetic Measurements.—Except in determination of the order with respect to each reactant in the triethylsilane–iodine reaction, initial concentrations of the reactants were accurately equal (usually 0·05—0·01M). Runs were usually carried out in sealed tubes containing 10 ml. of liquid, protected from light (Al foil). Tubes were broken under aqueous potassium iodide and

the iodine was quickly extracted from the organic layer by shaking. (If the shaking was delayed, reaction proceeded at a normal rate in the organic layer.)

Faster reactions were carried out in an amber-glass vessel with ground stopper, samples (including some to give the " initial " concentration after the mixture had reached the thermostat temperature) being withdrawn by pipette. Determinations of acid for these runs were significant only up to the saturation concentration.

Titration of iodine by thiosulphate was followed by determination of the acid, either with alkali, or, more usually, by titration of iodine liberated on adding excess of potassium iodate; the acid includes that produced by hydrolysis of organosilicon iodide.

Rate constants within a run were calculated according to the equation $k_4 = (1/3t)[1/(a-x)^3 - 1/a^3]$, where a is the initial concentration of the reactants, and $(a - x)$ the concentration of iodine after time t. The rate constants quoted in the discussion were obtained from the slope of the straight-line plot of $1/(a - x)^3$ against t. An error in iodine determination is greatly magnified in the rate constant, and the rate constants quoted may be in error by as much as $\pm 10\%$, although much better agreement than this was often obtained within a run and for duplicates.

Typical runs follow; the " iodine titre " is the amount of 0·025N-sodium thiosulphate solution required to discharge the iodine, and the " acid titre " is the amount to discharge the additional iodine produced on subsequent addition of potassium iodate. The sum of the " iodine titre " and " acid titre " should remain constant in a run according to eqn. (1).

Triethyliodosilane in carbon tetrachloride at 25°.

(Initially, $[I_2] = [Et_3SiH] = 0{\cdot}025$M; in tubes.)

Time, hr.	0	1/2	1	2	3	4	5	10	15	20	50	100
Iodine titre, ml.	10·00	9·22	8·65	7·90	7·35	6·50	6·00	5·42	4·84	4·44	3·35	2·66
Acid titre, ml.	0	0·60	1·30	2·00	2·45	3·40	3·95	4·55	5·10	5·55	6·55	7·35
$10^{-3} k_4$	—	11·7	11·7	10·8	10·7	11·0	11·2	11·2	11·3	11·0	10·9	11·1

From graph, $k_4 = 11{\cdot}3 \times 10^3$ mole^{-3} l.^{3} hr.$^{-1}$.

*Tri-*n*-propylsilane in benzene at 25°.*

(Initially, $[I_2] = [Pr_3SiH] = 0{\cdot}0234$M; in stoppered vessel.)

Time, min.	0	6	11	31	45	57	111	151
Iodine titre, ml.	9·32	8·56	8·21	7·12	6·60	6·22	5·29	4·67
Acid titre, ml.	0·75	0·45	1·75	2·85	—	—	—	—
$10^{-3} k_4$	—	76·6	67·2	63·5	63·6	65·6	63·7	67·8

From graph, $k_4 = 63{\cdot}6 \times 10^3$ mole^{-3} l.^{3} hr.$^{-1}$.

Triethyliodosilane and Iodine in Carbon Tetrachloride.—The reaction was of fourth order within a run and the rate constant was independent of the initial concentration within the limited range which could be studied :

Initial concn. of each reactant, M	0·0166	0·025	0·033
$10^{-3} k_4$ at 25°	11·3	11·3	10·5

Various unequal initial concentrations of iodine and silane (mole ratios 2 : 1 to 1 : 2) were used to determine the order with respect to each reactant. The slopes of the curve $[I_2]$ against t at various points were compared with those calculated, by using k_4 given above, for the expressions, $-d[I_2]/dt = k_4[Et_3SiH]^y[I_2]^{4-y}$, and y was shown clearly to be unity.

Additions were made to 10-ml. quantities of the " standard " reaction mixture (initially $I_2 = Et_3SiH = 0{\cdot}025$M) at 25°, and iodine was determined at intervals up to 7 hr. Water (0·05 g.), broken glass (equivalent to twice the surface area of the reaction vessel), or glass-wool (giving a large increase in surface area) did not affect the rate of reaction. (When moisture was present a brown deposit formed on the walls but disappeared in later stages of the reaction.) Activated alumina (0·5 g. of 200-mesh) caused a definite rate increase (*e.g.*, 60% reaction in 2 hr. compared with the usual 22% reaction). α-Picoline (either 0·05 or 0·1 g.) caused immediate loss of iodine colour when the reactants were mixed, with formation of a brown deposit containing 49—50% of the original iodine ($CH_3{\cdot}C_5H_4{\cdot}NHI,I_2$?). Ethanol (0·05 g.) caused a fast immediate reaction removing 52—46% of the original iodine, followed by a slower reaction.

Exposure to daylight and to a 100-watt lamp caused no change in rate over the first 40% of reaction. (The reaction products are decomposed by light, but relatively slowly. If a sealed tube containing reaction mixture is exposed to daylight for some weeks all the iodine returns.)

Hydrogen iodide (0·025M) or triethyliodosilane (0·025M) did not affect the rate. A mixture of triethyliodosilane (0·025M) and hydrogen iodide (0·025M) in carbon tetrachloride at 25° in tubes protected from light did not change in iodine or acid content during 10 days.

The rate was unchanged by bubbling oxygen or nitrogen through the reaction mixture for 30 sec. before the tubes were sealed, or by repeated freezing and pumping-out of the reactant solutions before mixing. When the reaction mixture was cooled to −80° and then quickly warmed to room temperature the iodine was almost completely removed; this could be caused by the increase in reactant concentrations as the solvent freezes.

Triethylsilane and Iodine in Dioxan and Nitrobenzene.—The iodine colour faded rapidly, but not completely, as equal volumes of triethylsilane (0·05M) and iodine (0·05M) in dioxan were mixed at room temperature (*ca.* 18°). About 10% of the iodine was present after 1 min., but iodine returned fairly rapidly. Titration within 1 min. of mixing equal volumes of triethylsilane (0·025M) and iodine (0·025M) in nitrobenzene at *ca.* 18° showed 50% of the iodine to be present; this increased to 80% after 40 min.

Trichlorosilane and Halogens.—Trichlorosilane in carbon tetrachloride in contact with aqueous potassium iodide produces a substance which removes iodine in the aqueous layer, and so tubes were broken under aqueous potassium iodide containing a slight deficiency of sodium thiosulphate. Trichlorosilane (0·025M) did not react detectably (<1%) with iodine (0·025M) in carbon tetrachloride or chloroform in 40 hr., or with bromine (0·025M) in carbon tetrachloride in 10 hr.

Triethylsilane and Iodine Monochloride.—When equal volumes of iodine monochloride (0·05M) and triethylsilane (0·05M) in carbon tetrachloride were mixed the colour changed immediately from brown to iodine-violet. Titration completed within 1 min. of mixing showed that 50% ± 0·5% of the halogen had been removed. Subsequently, halogen disappeared at the rate expected for the triethylsilane–iodine reaction. Dry nitrogen, bubbled through the mixture, carried off hydrogen chloride but no detectable hydrogen iodide in the first hour.

The brown colour changed immediately to iodine-violet when equal volumes of carbon tetrachloride solutions of iodine monochloride (0·05M) and triethyliodosilane (0·05M) or hydrogen iodide (0·05M) were mixed, and only hydrogen chloride was carried from the latter mixture by nitrogen.

Triphenylsilane and Bromine.—A mixture of bromine (0·025M) and triphenylsilane (0·025M) in carbon tetrachloride contained 60% and 46% of the bromine after *ca.* 1 and 2 min., respectively, at 18°, and 33% after 2 and 45 hr. at 25°. When change in bromine concentration was followed in an absorptiometer the results agreed well with those from the titration method.

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Reaction of Nitric Oxide with Gaseous Hydrocarbon Free Radicals. Part II. Radicals produced by Pyrolysis of Di-n-butylmercury.*

By H. T. J. Chilton and B. G. Gowenlock.

[Reprint Order No. 5293.]

The products of pyrolysis of di-*n*-butylmercury in a flow system with nitrogen and nitric oxide as carrier gas have been studied. It is shown that a mixture of an oxime and a nitroso-compound is produced. The properties of this mixture are compared with those for the *iso*propyl radical reaction, and correlations with the monomeric and the dimeric state of aliphatic nitroso-compounds are drawn. The reaction products with nitrogen as carrier gas are also reported.

It has been established (*J.*, 1953, 3232) that *iso*propyl radicals react with nitric oxide to give a nitroso-compound and acetoxime. It has also been shown that perfluoroalkyl radicals and nitric oxide give deep blue perfluoroalkyl nitroso-compounds (Haszeldine, *ibid.*, p. 2075; Banus, *ibid.*, p. 3755). Gingras and Waters (*Chem. and Ind.*, 1953, 615) have established that nitric oxide reacts with 2-cyano-2-propyl radicals in benzene solution. It has also been established that alkoxy-radicals can react with nitric oxide (Mortlock and Style, *Nature*, 1952, **170**, 706; Levy, *J. Amer. Chem. Soc.*, 1953, **75**, 1801) to give the alkyl nitrite. It has been pointed out to us that Raley, Rust, and Vaughan (*ibid.*, 1948, **70**, 88) isolated formaldoxime after thermal decomposition of di-*tert.*-butyl peroxide in the presence of nitric oxide, probably from the reaction sequence $CH_3\cdot + NO \longrightarrow CH_3\cdot NO \longrightarrow H_2C{:}N\cdot OH$. It appears, therefore, that the simpler radicals react with nitric oxide to form an addition product.

Nitroso-compounds have been prepared by Tarte (*Bull. Soc. roy. Liége*, 1953, **22**, 226) by the original photolytic method of Coe and Doumani (*J. Amer. Chem. Soc.*, 1948, **70**, 1516). The preparation of nitrosomethane is described, and other nitroso-paraffins (probably nitrosoethane) which are liquid at room temperature are reported.

Experimental

Reaction in the Presence of Nitric Oxide.—The experimental technique was essentially that used for the work with di*iso*propylmercury, pyrolyses being performed in the temperature range 376—410°. Di-*n*-butylmercury (B.D.H.) was purified by repeated bulb-to-bulb distillation under a high vacuum until a product of constant vapour pressure was obtained. The partial pressure of the di-*n*-butylmercury in the reaction vessel was about 0·016 mm. in all the runs; this is lower by a factor of about 8 than that for di*iso*propylmercury. The products of the pyrolysis were trapped in a U-tube at −78°, and two traps in series at −130° and −183° severally. Nitric oxide was consumed during pyrolysis at a rate varying from 0·03 to 0·1 mm./min. and was therefore added at intervals from the reservoir to keep the pressure in the reaction vessel constant to within ±0·2 mm. On the completion of a run the U-tube contained mercury together with undecomposed di-*n*-butylmercury, the −130° trap contained a yellow solid and a colourless liquid (probably hydrocarbons), whereas the −183° trap contained a little yellow solid together with some hydrocarbon. The technique established in Part I was then used for determining the m. p. of the yellow solid; it melted in the range −60° to −55° to a yellow-brown liquid which speedily changed into a white solid. All other products were pumped off from the white solid under a vacuum and the solid was then examined. A small amount of a relatively involatile liquid remained and the ultra-violet absorption spectrum of this was obtained.

Experiments with the white solid. Chemical tests were made for nitroso- and oxime groups (Feigl, "Spot Tests," Elsevier, Amsterdam, 1939). Liebermann's nitroso-test (*op. cit.*, p. 267) gave a green colour, the product becoming green-yellow in sodium hydroxide solution. The oxime test (*op. cit.*, p. 291) gave a pink colour, and when the solid was fused with diphenylamine, and concentrated sulphuric acid was added, a blue colour resulted (Coe and Doumani, *loc. cit.*).

* Part I, *J.*, 1953, 3232.

A sample of nitrosomethane prepared according to the method of Coe and Doumani also gave a green colour in the Liebermann test.

Investigations of the ultra-violet absorption spectra of solutions of the solid were made with a Unicam SP. 500 photoelectric quartz spectrophotometer. As the composition of the substance was unknown, only the data for $\lambda_{max.}$ in dilute solutions are presented, no determination of ε values being made. The values obtained are given in Tables 1 (aqueous solutions) and 2 (ethereal solutions). It is noteworthy that the $\lambda_{max.}$ values were unaltered by the substitution

TABLE 1.

Substance	$\lambda_{max.}$ (mμ)	Substance	$\lambda_{max.}$ (mμ)
Solid	<200, 267	Acetaldoxime [a]	203
Solid + HCl	<200, 267	Butyraldoxime [b]	<200
Nitrosomethane	266—267	*iso*Propyl solid [c]	<200, 266

[a] Prepared by usual methods. [b] Product from L. Light & Co. [c] Part I.

of a silica trap at −130° for the Pyrex trap. A specimen of the solid, kept under a vacuum in a small Pyrex tube and in the dark, soon became moist and within a day completely melted. After 8 weeks the presence of a small quantity of crystals on the walls of the tube was noticed. In ether the crystals showed peaks at 208 and 289 mμ, and the liquid at 207 and 288—289 mμ. Thus any separation achieved by this method was slight and this contrasts with the *iso*propyl case.

Other specimens of the solid were sealed off under a vacuum and submitted to microanalysis (Weiler and Strauss): low values for nitrogen were obtained unless the method of analysis was modified by using Friederich's micro-Kjeldahl method with hydriodic acid as noted by Coe and

TABLE 2.

Substance	$\lambda_{max.}$ (mμ)	Substance	$\lambda_{max.}$ (mμ)
Solid (Pyrex trap)	209, 289—290	Acetaldoxime	211—212
Solid (silica trap)	210, 289	Butyraldoxime	212
Nitrosomethane	287	U-Tube washings	209, 211, 290 (Infl. 250—255)
*iso*Propyl solid [a]	209—211, 289—292, 665	Di-*n*-butylmercury	211—212, (Infl. 250—255)
Liquid in −130° trap	210—212, 289—290	2-Methyl-2-nitrosopropane	300,[b] 665,[b] 296,[c] 675 [c]

[a] Part I. [b] Baly and Desch, *J.*, 1908, **93**, 1752. [c] Jander and Haszeldine, *J.*, 1954, 912.

Doumani (*loc. cit.*) (Found: C, 39·1; H, 8·4; N, 21·7. Calc. for C_2H_5ON: C, 40·7; H, 8·5; N, 23·7. Calc. for C_4H_9ON: C, 55·2; H, 10·1; N, 16·1%). The solid, when freshly prepared, was a white waxy substance with a sweet penetrating smell. It melted over the range 58—62° to a blue liquid which became a pale blue green as the temperature rose. The liquid charred at about 138°.

The behaviour of the solid in various solvents was investigated and the appearance of colours on dissolving, on gentle warming, and on boiling, was noted. The colour that appeared on dissolution faded completely, the rate of disappearance varying with the solvent. Benzene, ethyl acetate, acetic acid, and ethanol solutions all gave a colour on boiling that could not be regenerated by further heating. In all other cases, reheating reproduced the colour, albeit very faintly in some cases. The results are given in Table 3.

Reaction in the Absence of Nitric Oxide.—A number of experiments were performed in which nitrogen was used as the carrier gas, the experimental method being similar to that used by us for di*iso*propylmercury (*Trans. Faraday Soc.*, 1953, **49**, 1451), the trap temperatures being −50°, −130°, and −196°. The velocity constant, k, was determined from the mercury produced (trapped out at −50°), the relation being $d[Hg]/dt = k[Bu^n_2Hg]$. The velocity constant was unaltered in the presence of nitric oxide, suggesting the absence of a chain reaction, and the temperature dependence was given by the expression $\log_{10} k$ (sec.$^{-1}$) = 15·02 − 45,600/2·303RT, all experiments being carried out at a total pressure of about 4·4 mm. The hydrocarbons condensed in the −130° and −196° traps were estimated by expansion into spaces of known volumes and fractional volatilisation by use of baths at different temperatures; where possible, samples were analysed for unsaturated compounds by Melville and Robb's method (*Proc. Roy. Soc.*, 1949, *A*, **196**, 445), and in the case of C_6 and C_8 hydrocarbons the samples were weighed.

The results were only approximate, the molar ratios of the hydrocarbons produced being of the order $C_2 : C_4 : C_6 : C_8 = 6 : 1 : 1 : 0{\cdot}1$. The quantities of C_3 compound produced were always very small; any C_5 or C_7 hydrocarbons produced were included with the C_6 and C_8 respectively.

TABLE 3.

Solvent	B. p.	ε	Colour * of solution on: dissolving	gentle heating	boiling
n-C_5H_{12}	36°	1·85		(Insoluble)	
n-C_6H_{14}	69	1·91		(Insoluble)	
CCl_4	77	2·22	—	—	—
Dioxan	101	2·24	—	B—G	B—G
C_6H_6	80	2·30	B—G	B—G	B—G
PhMe	111	2·38	B	—	B
Et_2O	35	4·36	B	—	—
$CHCl_3$	61	4·64	B	B	B
$CHBr_3$	150	4·73	—	—	—
EtOAc	77	6·11	B	—	B
AcOH	118	6·13	—	—	B—G
CH_2Cl_2	40	9·14	B	—	B—G
$COMe_2$	56	21·45	—	B	B
EtOH	78	25·8	—	—	B
Pr^nNO_3	131	~30	—	B—G	B—G
$CH_3{\cdot}CN$	82	37·5	—	B—G	B—G
H_2O	100	80	—	—	—

* B = Blue, B—G = Blue-green.

The percentage unsaturation of the C_2 fraction was between 80 and 100% and of the C_4 fraction between 10 and 23%. Frey and Hepp (*J. Amer. Chem. Soc.*, 1933, **55**, 3357) give ethylene and n-butane as the principal gaseous products of the pyrolysis of di-n-butylmercury in a flow system. Our hydrocarbon balance was within 5% of the theoretical value.

DISCUSSION

The solid product formed on pyrolysis of di-n-butylmercury in nitric oxide at 376—410° is evidently a mixture of an oxime and a nitroso-compound. The pyrolysis reactions in the absence of nitric oxide are probably:

$$Bu^n{}_2Hg \longrightarrow 2Bu^n + Hg \quad . \; . \; . \quad (1)$$

$$2Bu^n \longrightarrow C_8H_{18} \quad . \; . \; . \; . \quad (2)$$

$$2Bu^n \longrightarrow C_4H_{10} + C_4H_8 \quad . \; . \quad (3)$$

$$Bu^n \longrightarrow Et + C_2H_4 \quad . \; . \; . \quad (4)$$

$$2Et \longrightarrow C_4H_{10} \quad . \; . \; . \; . \quad (5)$$

$$2Et \longrightarrow C_2H_4 + C_2H_6 \quad . \quad (6)$$

$$Bu^n + Et \longrightarrow C_6H_{14} \quad . \; . \; . \quad (7)$$

Such a reaction scheme would account for the products observed. The first step may involve the production of the radical Bu^nHg which then decomposes, though the similarity of the frequency factor to those for di*iso*propylmercury (Chilton and Gowenlock, *loc. cit.*) and di-n-propylmercury (*idem*, to be published) suggests that the two-bond fission is more likely. In the presence of nitric oxide the reactions

$$Bu^n + NO \longrightarrow Bu^n{\cdot}NO \quad . \; . \; . \quad (8)$$

$$Et + NO \longrightarrow Et{\cdot}NO \quad . \; . \; . \quad (9)$$

with subsequent partial isomerization to the oxime are suggested. Our analytical results suggest that mainly nitrosoethane and acetaldoxime are obtained, and this conclusion is that expected from consideration of the hydrocarbon products in the absence of nitric oxide. It may also be noted that the penetrating odour of butyraldoxime was absent from our product.

Many of the detailed results are analogous to those for the *iso*propyl case and similar interpretation of the results can thus be made. The melting of the yellow solid at −60° to −55° and its subsequent transition to a white solid we ascribe to the sequence: nitrosoalkane monomer (solid) ⟶ nitrosoalkane monomer (liquid) ⟶ nitrosoalkane dimer (solid). The oxime transition suggested by us in Part I has since been disproved experimentally, since no yellow colours were observed in the traps when acetoxime was passed through the reaction vessel under normal reaction conditions.

The ultra-violet absorption spectra are noteworthy. The good correlation with nitrosomethane strengthens the case for identification of the 266—267 mμ peak (aqueous solution) and 287—292 mμ peak (ethereal solution) with a dimeric nitroso-compound. The values of 300 and 665 mμ given by Baly and Desch (*loc. cit.*) and 296 and 675 mμ given by Jander and Haszeldine (*loc. cit.*) for 2-methyl-2-nitrosopropane and of 650—710 mμ for unimolecular halogenated nitrosoalkanes (Hammick and Lister, *J.*, 1937, 489; Lewis and Kasha, *J. Amer. Chem. Soc.*, 1945, **67**, 994) provide no argument against such an identification. No value for the absorption peak in the visible region was taken for ethereal solutions because fading was too rapid, but as the solution was blue the absorption was probably in the 650—710 mμ range. It is noteworthy that nitrosomethane dimer, which does not give a blue colour on dissolution in ether, gives an absorption maximum almost identical with those for compounds isolated in this (and the previous) investigations.

It might be argued that the failure to give the Liebermann colours is a reason for discounting the formation of a nitroso-compound; however, although tertiary aliphatic nitroso-compounds give this test (Bamberger and Seligman, *Ber.*, 1903, **36**, 685), yet nitrosomethane fails to give it. We suggest that Coe and Doumani's diphenylamine test (*loc. cit.*) is a better general test for primary and secondary aliphatic nitroso-compounds than the Liebermann test.

The behaviour of the solid when dissolved in various solvents is similar to that in the *iso*propyl case. The simplest feature is that of colour production on boiling, which is probably a temperature effect, being given by all solvents boiling above 40° with the exception of carbon tetrachloride, bromoform, and water. The last two solvents showed the same exceptional behaviour in the *iso*propyl case. It is worthy of note that no nitroso-compound gives a blue colour in aqueous solution. The colour change on dissolution occurs only in the solvents of low dielectric constant, the range being somewhat similar to those reported in Part I.

TABLE 4.

Compound	Colours on dissolution	Colours on heating solid	Colours on heating soln.	$\lambda_{max.}$ (mμ) Ether	$\lambda_{max.}$ (mμ) Water [a]	Colour at −130°
Me·NO	Colourless	Transient blue (>122°) few degrees above m. p.	Blue in toluene (110°)	287 —	266—267 —	Not yet investigated
Et·NO	Either colourless or immediate blue becoming colourless	Blue (>58—62°)	Blue (>40°) in certain solvents	289—290 —	267 —	Yellow : transition −60° to −55°
Pr^{i}·NO ...	Either colourless or immediate blue becoming colourless	Blue-green (>85—95°)	Blue (>80°) in certain solvents	290 665	266 —	Yellow : transition −85° to −78°
Bu^{t}·NO ...	Colourless, slowly becoming blue	Blue (>76°)	Immediate blue colour, blue on cooling	300, 296 665, 675	— —	Not yet investigated

[a] Aqueous solutions are all colourless.

There is now sufficient evidence to show that simple nitrosoalkanes exist and that isomerization to oximes is not instantaneous. The evidence for this misunderstanding is based upon some papers published fifty years ago which expressed the *opinion* that speedy isomerization occurred at room temperature (cf. Schmidt, *Ber.*, 1902, **35**, 2323; Bamberger and Seligman, *Ber.*, 1903, **36**, 685, 701). This opinion has been treated as fact for many years and should now be abandoned in the light of the work by Coe and Doumani (*loc. cit.*), Tarte (*loc. cit.*), and the present authors (*loc. cit.*). In this connection it is necessary to point out that nitroso-compounds are reasonably stable in the gas phase at 230—280° (*iso*propyl) and 376—410° (present investigation). The misconception concerning isomerization (the nitroso–hydroxyimino-system) is probably based on an analogy with the behaviour of nitrolic acids and nitrosoacetone, which isomerize rapidly. It should be noted that halogenonitrosoparaffins containing secondary hydrogen atoms and α-nitroso-

esters only isomerise slowly, and phenylnitrosomethane isomerises extremely slowly (cf. Sidgwick, " The Organic Chemistry of Nitrogen," Oxford, 1945, pp. 204—226).

The general properties of simple nitrosoalkanes are summarised in Table 4. The evidence available suggests an increasing stability of the monomeric state R·NO in the series R = Me < Et~ Pr^i < Bu^t, a blue-green colour being associated with nitroso-monomer, the dimer being colourless.

Studies of the reaction products of other free radicals with nitric oxide are in progress, and we are also investigating the preparation, properties, and structure of pure nitrosoalkanes. These will be reported later.

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Steroids and Walden Inversion. Part XIV. 5-Hydroxycholestane-3β-carboxylic Acid and Related Compounds.*

By G. ROBERTS, C. W. SHOPPEE, and R. J. STEPHENSON.

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Cholest-5-ene-3β-carboxylic acid and its methyl ester react with perbenzoic acid to give principally a 5α : 6α-epoxide. This, by reduction with lithium aluminium hydride and oxidation of the resulting diol, is converted into 5-hydroxycholestane-3β-carboxylic acid, which furnishes a 5α-hydroxy-anhydride with acetic anhydride and regenerates cholest-5-ene-3β-carboxylic acid by ionic dehydration.

Oxidation of methyl cholest-5-ene-3β-carboxylate with peracetic acid, or acetolysis of the above 5α : 6α-epoxide, gave methyl 6β-acetoxy-5-hydroxycholestane-3β-carboxylate, smoothly dehydrated to methyl 6β-acetoxycholest-4-ene-3β-carboxylate. This ester with perbenzoic acid gave only a single epoxide, shown to be the 4α : 5α-epoxide by conversion into 5-hydroxy-6-oxocholestane-3β-carboxylic acid, which by treatment with acetic anhydride yielded a 5α-hydroxy-anhydride.

CHOLEST-5-ENE-3β-CARBOXYLIC ACID (IV; R = H) reacts with perbenzoic acid, to give apparently a single epoxy-acid (VI; R = H), characterised as the methyl ester. Methyl cholest-5-ene-3β-carboxylate (IV; R = Me), however, and perbenzoic acid furnish a mixture of epimeric epoxy-esters. The major component, readily obtained pure by chromatography, is formulated as methyl 5 : 6α-epoxycholestane-3β-carboxylate (VI; R = Me) on the basis of optical rotatory evidence and by analogy with the major products of peroxidation of cholesterol (Plattner, Petrzilka, and Lang, *Helv. Chim. Acta*, 1944, **27**, 513, 1872) and *epi*cholesterol (Fudge, Shoppee, and Summers, *J.*, 1954, 958; Plattner, Fürst, Koller, and Kuhn, *Helv. Chim. Acta*, 1954, **37**, 258). Reduction of the epoxy-acid (VI; R = H) or of the epoxy-ester (VI; R = Me) with lithium aluminium hydride gave the diol (III), of which only the primary hydroxyl group was oxidised by chromium trioxide to yield 5-hydroxycholestane-3β-carboxylic acid (II; R = H). The methyl ester (II; R = Me) by dehydration with thionyl chloride–pyridine at 20° regenerated methyl cholest-5-ene-3β-carboxylate (IV; R = Me); the acid (II; R = H) by dehydration with acetic anhydride at 140° gave the anhydride (I), which by alkaline hydrolysis regenerated the acid (II; R = H).

The structure (I) is supported by infra-red spectroscopic evidence. The spectrum of a Nujol mull of the acid (II; R = H) shows peaks at 3560 (free hydroxyl), 3300—2500 (associated hydroxyl group of carboxylic acid) and 1702 $cm.^{-1}$ (carbonyl group of carboxylic acid); the spectrum of the methyl ester (II; R = Me) in carbon disulphide solution shows peaks at 3570 (free hydroxyl) and at 1735 and 1165 $cm.^{-1}$ (carboxylic ester). The anhydride

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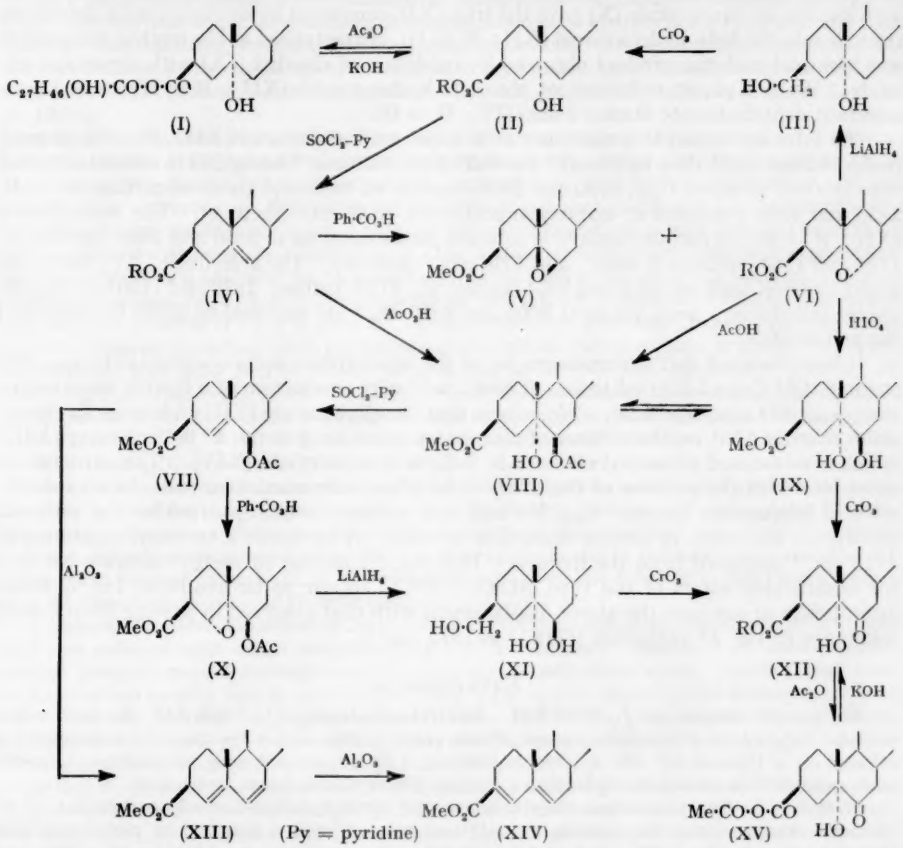
(I) in carbon disulphide solution exhibited peaks at 3560 (free hydroxyl) and at 1810 and 1743 cm.$^{-1}$ (carboxylic anhydride). In Nujol, the peaks appeared at 3540, 1787, and 1730 cm.$^{-1}$ respectively.

The formation of the anhydride (I) demonstrates the *trans*-relationship of the carboxyl and the hydroxyl group in the acid (II; R = H), and confirms the β-configuration assigned to the $C_{(3)}$-carboxyl group in Marker's acid (IV; R = H) (Shoppee and Stephenson, *J.*, 1954, 2230; Roberts, Shoppee, and Stephenson, *ibid.*, p. 2705), because a *cis*-arrangement would have furnished a γ-lactone (cf. Shoppee, *J.*, 1948, 1032). It seemed of interest in



this connection to attempt to prepare 5-hydroxycoprostane-3β-carboxylic acid and to examine its behaviour on dehydration.

The preparation of 5β-hydroxy-steroids has been achieved (*a*) in 20% yield by reduction of 5β : 6β-epoxysteroids with lithium aluminium hydride (Plattner, Heusser, and Feurer, *Helv. Chim. Acta*, **1949**, **32**, 587) and (*b*) smoothly and in excellent yield by reduction of 4β : 5β-epoxy-steroids with the same reagent (Plattner *et al.*, *ibid.*, 1948, **31**, 1822, 1888; 1949, **32**, 266, 1070). Since the 5β : 6β-epoxy-ester (V) was formed in small quantity only, and was not isolated in a state of purity, a Δ^4-steroid suitable for preparation of a 4β : 5β-epoxide was obtained as follows. Methyl cholest-5-ene-3β-carboxylate (IV; R = Me) was treated with peracetic acid to give mainly the diol monoacetate (VIII) with some of the diol (IX); alternatively, acetolysis of the mixture of epoxy-esters (V + VI; R = Me) gave the diol monoacetate (VIII), whilst hydration of the pure epoxy-ester (VI; R = Me) with

periodic acid yielded the diol (IX), converted by treatment with acetic anhydride into the diol monoacetate (VIII). Subsequently, it was found that performic acid was more effective, and that the mixture of diol monoformate (as VIII) and diol (IX) could be separated chromatographically or hydrolysed with methanolic hydrogen chloride to the diol (IX). Dehydration of the diol monoacetate (VIII) with thionyl chloride–pyridine gave methyl 6β-acetoxycholest-4-ene-3β-carboxylate (VII).

By contrast with the results of Plattner *et al.* (*loc. cit.*), the unsaturated ester (VII) with perbenzoic acid gave only a single 4 : 5-epoxide, which was shown to be methyl 6β-acetoxy-4α : 5α-epoxycholestane-3β-carboxylate (X). By reduction with lithium aluminium hydride, the 4α : 5α-epoxide (X) gave the triol (XI), converted by oxidation with chromium trioxide into the keto-hydroxy-acid (XII; R = H), characterised as the methyl ester which was identical with the product obtained by oxidation of the diol (IX) with chromium trioxide. Wolff–Kishner reduction of the keto-hydroxy-acid (XII; R = H) caused concomitant dehydration to Marker's acid (IV; R = H).

The infra-red absorption spectrum of a Nujol mull of the acid (XII; R = H) showed peaks at 3430 cm.$^{-1}$ (free hydroxyl; the shift from 3550 cm.$^{-1}$ being due to vicinal action of the carbonyl group at $C_{(6)}$), 2990 and 2820 (associated hydroxyl group of carboxylic acid), 1735 and 1250 (carbonyl of carboxylic acid), and 1695 cm.$^{-1}$ (ketone). The methyl ester (XII; R = Me) in carbon disulphide solution shows maxima at 3550 and 3440 (hydroxyl), 1735 and 1165 (carboxylic ester), and 1710 cm.$^{-1}$ (ketone). The anhydride (XV) in a Nujol mull exhibited peaks at 3500 and 3404 (hydroxyl), 1710 (ketone), 1812 and 1730 cm.$^{-1}$ (carboxylic anhydride); weak peaks at 3000 and 2820 cm.$^{-1}$ are ascribed to slight hydrolysis of the anhydride.

It was observed that chromatography of the unsaturated acetoxy-ester (VII), $\lambda_{max.}$ 208 mμ in EtOH (log ε 3·32), led to loss of acetic acid with production of a doubly unsaturated ester, $\lambda_{max.}$ 274 mμ (log ε 4·26). We believe that the allyl acetate (VII) undergoes an elimination reaction (*E*1) on the column of aluminium oxide to give the 4 : 6-diene ester (XIII) which is isomerised to methyl cholesta-3 : 5-diene-3-carboxylate (XIV). This structure is consistent with the position of the ultra-violet absorption maximum (calc. for an αγδ-substituted conjugated dienone: $\lambda_{max.}$ 266 mμ), and appears to be supported by the infra-red absorption spectrum in carbon disulphide solution. This shows a carbonyl maximum at 1712 cm.$^{-1}$ displaced from the frequency 1735 cm.$^{-1}$ common to methyl esters. No data for unsaturated esters of the type RO·CO·C:C·C:C appear to be available, but it seems appropriate to compare the above displacement with that observed in passing from steroid 3-ketones to the Δ^4-analogues (1718 ⟶ 1675 cm.$^{-1}$).

Experimental

For general details see *J.*, 1953, 243. Neutralised alumina (*J.*, 1953, 543) was used where stated. $[\alpha]_D$ are in chloroform except where noted; ultra-violet spectra were determined in ethanol on a Unicam SP 500 spectrophotometer, with a corrected scale, and infra-red spectra were examined in carbon disulphide on a Perkin–Elmer double-beam instrument.

Methyl 5 : 6α-*Epoxycholestane*-3β-*carboxylate.*—(*a*) Methyl cholest-5-ene-3β-carboxylate (2 g.) (Roberts, Shoppee, and Stephenson, *loc. cit.*) was treated with a solution of perbenzoic acid (1·1 mol.) in chloroform (50 c.c.) for 48 hr. at 15°. The solution was diluted with ether, and excess of perbenzoic acid destroyed by repeated washing with sodium iodide solution; after further washing with solutions of sodium thiosulphate and chloride, the product was isolated in the usual way and chromatographed on a column of aluminium oxide (60 g.) prepared in pentane. Elution with benzene–pentane (1 : 9, 11 × 200 c.c.; 2 : 3, 2 × 200 c.c.) gave a solid (total 1·4 g.); all fractions were identical. *Methyl* 5 : 6α-*epoxycholestane*-3β-*carboxylate*, recrystallised from methanol, had m. p. 80°, $[\alpha]_D$ −30° (*c*, 2·0) [Found (after drying at 15°/0·01 mm. for 15 hr.): C, 78·3; H, 10·9. $C_{29}H_{48}O_3$ requires C, 78·3; H, 10·9%]. Further elution with benzene–pentane (2 : 3, 2 × 200 c.c.) furnished solid material, m. p. 62—80° (from methanol).

In a repetition, methyl 5 : 6α-epoxycholestane-3β-carboxylate was isolated by crystallisation from methanol–ethyl acetate. The mother-liquor material was chromatographed on aluminium oxide (30 g.) prepared in pentane. Elution with pentane afforded a trace of oil whilst benzene–pentane (2 : 3, 100 c.c.) gave a solid (66 mg.), which was crystallised from methanol, m. p. 76—86°. A further eluate (67 mg.) melted at 80—88° whilst use of ether (100 c.c.) afforded a

solid (374 mg.) which, recrystallised from methanol, had m. p. 76—85°, $[\alpha]_D$ +0·2° (*c*, 2·4), the change in optical rotation being due to the presence of methyl 5 : 6β-epoxycoprostane-3β-carboxylate.

(*b*) Cholest-5-ene-3β-carboxylic acid (2 g.) was treated with an excess of perbenzoic acid in chloroform at 15° for 40 hr. Working up gave a product which was esterified with ethereal diazomethane and chromatographed on aluminium oxide (30 g.) prepared in pentane. Elution with pentane (100 c.c.) furnished a trace of oil whilst further elution with pentane (400 c.c.), benzene–pentane (2 : 3, 500 c.c.), and benzene (200 c.c.) furnished methyl 5 : 6α-epoxycholestane-3β-carboxylate (total 1·64 g.); crystallised from methanol, this had m. p. 80°.

3β-*Hydroxymethylcholestan*-5-*ol*.—Methyl 5 : 6α-epoxycholestane-3β-carboxylate (2·5 g.) in ether (150 c.c.) was added to a solution of lithium aluminium hydride (2·5 g.) in ether (300 c.c.). After 2 hours' refluxing, excess of lithium aluminium hydride was destroyed by water, and the product isolated in the usual manner. The *diol*, crystallised several times from acetone, had m. p. 138—139° [Found (after sublimation) : C, 80·2; H, 11·9. $C_{28}H_{50}O_2$ requires C, 80·3; H, 12·0%].

5-*Hydroxycholestane*-3β-*carboxylic Acid*.—The foregoing product (1 g.) in acetic acid (50 c.c.) was treated with a 2% solution of chromium trioxide in 98% acetic acid (50 c.c.) at 15° for 16 hr.; the solution was diluted, acidified with 2N-sulphuric acid, and extracted with ether. Washing the ether extracts with 2N-sodium carbonate removed acetic acid and precipitated sodium 5-hydroxycholestane-3β-carboxylate; this was filtered off and the free acid obtained by shaking the sodium salt with ether–2N-sulphuric acid. The acid was esterified with ethereal diazomethane, and the ester was introduced on to a column of aluminium oxide (25 g.) in pentane. Elution with benzene–pentane (1 : 4, 2 × 100 c.c.) afforded only a trace of material, whilst further elution with benzene–pentane (1 : 1, 4 × 100 c.c.), benzene (100 c.c.), and ether (100 c.c.) gave *methyl* 5-*hydroxycholestane*-3β-*carboxylate* (1 g.), which was crystallised from methanol as plates, m. p. 113°, $[\alpha]_D$ +18° (*c*, 2·9), +21° (*c*, 1·0) [Found (after drying at 20°/0·01 mm. for 16 hr.) : C, 77·8; H, 11·4. $C_{29}H_{50}O_3$ requires C, 77·95; H, 11·3%]. 5-*Hydroxycholestane*-3β-*carboxylic acid*, obtained by hydrolysis with methanolic N-potassium hydroxide and recrystallised from methanol, had m. p. 211—213°, $[\alpha]_D$ +19° (*c*, 1·0) [Found (after drying at 60°/0·01 mm. for 6 hr.) : C, 77·2; H, 11·1. $C_{28}H_{48}O_3$ requires C, 77·7; H, 11·2%].

Methyl Cholest-5-*ene*-3β-*carboxylate*.—Methyl 5-hydroxycholestane-3β-carboxylate (43 mg.), dissolved in pyridine (1 c.c.), was treated at 0° with thionyl chloride (0·2 c.c.). After 10 min., the mixture was poured into water and the product (39 mg.) isolated in the usual manner. Chromatography on aluminium oxide (6 g.) with pentane as eluant furnished only traces of oil, whilst use of benzene–pentane (1 : 4, 100 c.c.) gave methyl cholest-5-ene-3β-carboxylate (38 mg.), m. p. and mixed m. p. 100—101° (from methanol).

5-*Hydroxycholestane*-3β-*carboxylic Anhydride*.—5-Hydroxycholestane-3β-carboxylic acid (200 mg.) was refluxed with acetic anhydride (12 c.c.) for 30 min. Removal of solvent under reduced pressure gave 5-*hydroxycholestane*-3β-*carboxylic anhydride* which, recrystallised from methanol–ethyl acetate, had m. p. 228—230°, $[\alpha]_D$ +15° (*c*, 0·8) [Found (after drying at 15°/0·01 mm.) : C, 79·3; H, 11·0. $C_{56}H_{94}O_5$ requires C, 79·4; H, 11·1%]. Hydrolysis with methanolic N-potassium hydroxide gave, after acidification and the usual extraction, 5-hydroxycholestane-3β-carboxylic acid, m. p. and mixed m. p. 210—213°.

Methyl 5 : 6β-*Dihydroxycholestane*-3β-*carboxylate*.—(*a*) Methyl cholest-5-ene-3β-carboxylate (10 g.) was suspended in formic acid (95%; 100 c.c.) and benzene (100 c.c.). Hydrogen peroxide (100-vol.; 100 c.c.) was added and the mixture stirred at 45° for 1 hr. Benzene was removed and, after cooling slowly during 2 hr., the solution was diluted with water, and the product extracted with ether, to furnish after the usual working up, an oil, a portion of which (1·8 g.) was chromatographed on aluminium oxide (40 g.) prepared in benzene. Elution with benzene (5 × 100 c.c.) gave an oil (214 mg.), whilst further elution with benzene (1 × 100 c.c.) and ether–benzene (1 : 19, 4 × 100 c.c.) gave a solid (1·1 g.) which was recrystallised from methanol to give *methyl* 6β-*formoxy*-5-*hydroxycholestane*-3β-*carboxylate* as prisms, m. p. 134—135°, $[\alpha]_D$ −17° (*c*, 1·7) [Found (after drying at 90°/0·03 mm. for 3 hr.) : C, 73·1; H, 10·2. $C_{30}H_{50}O_5$ requires C, 73·4; H, 10·3%]. Further elution with ether–benzene (1 : 4, 100 c.c.; 1 : 1, 100 c.c.) furnished a solid (350 mg.), which was recrystallised from methanol to give *methyl* 5 : 6β-*dihydroxycholestane*-3β-*carboxylate*, double m. p. 134°/151°, $[\alpha]_D$ +3° (*c*, 1·7) [Found (after sublimation at 180°/0·01 mm.) : C, 75·3; H, 10·8. $C_{29}H_{50}O_4$ requires C, 75·3; H, 10·9%]. The mixture of diol and its 6β-formyl derivative obtained from methyl cholest-5-ene-3β-carboxylate (10 g.) was partially hydrolysed by refluxing it with methanol (400 c.c.) and concentrated hydrochloric acid (15 c.c.). After 1 hr., the solution was diluted with water, and the product extracted with

ether, washed, dried, and evaporated to furnish methyl 5 : 6β-dihydroxycholestane-3β-carboxylate, double m. p. 134°/151°, after recrystallisation from methanol.

(*b*) Methyl 5 : 6α-epoxycholestane-3β-carboxylate (100 mg.) was refluxed for 45 min. with acetone (3 c.c.) and water (1 c.c.) containing periodic acid (64 mg.); the solution was diluted with water and extracted with ether, and the product isolated in the usual manner. Crystallisation from methanol gave methyl 5 : 6β-dihydroxycholestane-3β-carboxylate, double m. p. 133—134°/151°.

Methyl 6β-*Acetoxy*-5-*hydroxycholestane*-3β-*carboxylate*.—(*a*) Methyl cholest-5-ene-3β-carboxylate (26 g.) was dissolved in acetic acid (500 c.c.), and hydrogen peroxide (100-vol.; 50 c.c.) added to the solution maintained at 95°; a further addition of hydrogen peroxide (50 c.c.) was made after 0·5 hr. After a total period of 1·5 hr. at 95°, the mixture was poured into water, the product extracted with benzene and, after the usual washing, drying, and removal of solvent, the oil obtained was dissolved in pyridine (50 c.c.) and acetic anhydride (25 c.c.). After being kept at 15° for 15 hr., the mixture was diluted with water and extracted with ether, and after the usual washing, drying, and removal of solvent the product was crystallised from methanol to furnish *methyl* 6β-*acetoxy*-5-*hydroxycholestane*-3β-*carboxylate*, m. p. 173—175°, $[\alpha]_D$ −24° (*c*, 1·7) [Found (after drying at 15°/0·01 mm. for 15 hr.): C, 73·7; H, 10·2. $C_{31}H_{52}O_5$ requires C, 73·8; H, 10·4%].

(*b*) Methyl 5 : 6α-epoxycholestane-3β-carboxylate (2·2 g.) was refluxed in acetic acid (150 c.c.) with anhydrous potassium acetate (4 g.) for 2 hr.; the mixture was cooled and diluted with water, and the product isolated in the usual manner. Crystallisation from methanol furnished methyl 6β-acetoxy-5-hydroxycholestane-3β-carboxylate (2·1 g.), m. p. 174—176°, identical with the previous preparation. A similar experiment using the αβ-epoxide mixture gave analogous results.

(*c*) Methyl 5 : 6β-dihydroxycholestane-3β-carboxylate (11·5 g.), in benzene (100 c.c.) and pyridine (20 c.c.), was treated with acetic anhydride (20 c.c.) at 15° for 16 hr. The solvents were removed in a vacuum, the product was dissolved in ether, and the ethereal solution washed, dried, and evaporated to furnish methyl 6β-acetoxy-5-hydroxycholestane-3β-carboxylate, m. p. 173—175° (11·5 g.).

Methyl 6β-*Acetoxycholest*-4-*ene*-3β-*carboxylate*.—Methyl 6β-acetoxy-5-hydroxycholestane-3β-carboxylate (10·5 g.) in pyridine (100 c.c.) was treated with thionyl chloride (12 c.c.) at 0° for 15 min. Excess of thionyl chloride was destroyed by ice. Further dilution furnished a solid which was filtered off, washed, and crystallised from methanol to give *methyl* 6β-*acetoxycholest*-4-*ene*-3β-*carboxylate*, m. p. 122—123°, $[\alpha]_D$ +14° (*c*, 2·0), $\lambda_{max.}$ 208 mμ in EtOH (log ε 3·32) [Found (after drying at 15°/0·01 mm. for 15 hr.): C, 76·2; H, 10·3. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4%].

A solution of methyl 6β-acetoxycholest-4-ene-3β-carboxylate in pentane was introduced on to a column of aluminium oxide (Spence Type H, activity ~II). After 24 hr., elution with benzene–pentane (1 : 4) gave *methyl cholesta*-3 : 5-*diene*-3-*carboxylate* which, crystallised from methanol, had m. p. 88°, $[\alpha]_D$ −140° (*c*, 1·5), $\lambda_{max.}$ 274 mμ in EtOH (log ε 4·26) [Found (after drying at 20°/0·01 mm.): C, 81·2; H, 10·9. $C_{29}H_{46}O_2$ requires C, 81·6; H, 10·9%].

Methyl 6β-*Acetoxy*-4α : 5-*epoxycholestane*-3β-*carboxylate*.—Methyl 6β-acetoxycholest-4-ene-3β-carboxylate (7 g.) in chloroform (20 c.c.) was treated with perbenzoic acid (1·2 mol.) in chloroform (20 c.c.). After 36 hr. at 15°, the solution was diluted with ether, and the product isolated in the usual way to furnish *methyl* 6β-*acetoxy*-4α : 5-*epoxycholestane*-3β-*carboxylate*, which crystallised from methanol and then from ethyl acetate as needles, m. p. 141—143°, $[\alpha]_D$ +28° (*c*, 1·2) [Found (after drying at 15°/0·01 mm. for 15 hr.): C, 74·3; H, 10·3. $C_{31}H_{50}O_5$ requires C, 74·1; H, 10·1%].

3β-*Hydroxymethylcholestane*-5 : 6β-*diol*.—Methyl 6β-acetoxy-4α : 5-epoxycholest-4-ene-3β-carboxylate (2·2 g.) was refluxed with lithium aluminium hydride (2 g.) in ether (250 c.c.) for 1·5 hr., water was added, and the product isolated in the usual manner. Crystallisation from ether–pentane gave the *triol*, m. p. 188—189°, $[\alpha]_D$ +5° (*c*, 1·0) [Found (after sublimation at 200°/0·01 mm.): C, 77·4; H, 11·6. $C_{28}H_{50}O_3$ requires C, 77·4; H, 11·6%].

5-*Hydroxy*-6-*oxocholestane*-3β-*carboxylic Acid*.—(*a*) The triol (1 g.) in acetic acid (10 c.c.) was treated with chromium trioxide (0·67 g.) in acetic acid (33 c.c.) for 16 hr. at 25°, then the excess of chromium trioxide was destroyed by adding methanol. Dilution with water followed by extraction with ether, extraction of the acid with 2N-potassium hydroxide, and acidification and ether-extraction of the alkaline extracts furnished 5-*hydroxy*-6-*oxocholestane*-3β-*carboxylic acid* which, crystallised from pentane, had m. p. 246—250°, $[\alpha]_D$ −35° (*c*, 1·1) [Found (after drying at 40°/0·01 mm. for 15 hr.): C, 75·5; H, 10·3. $C_{28}H_{46}O_4$ requires C, 75·3; H, 10·4%]. The *methyl* ester, prepared by using ethereal diazomethane and crystallised from pentane,

had m. p. 152°, $[\alpha]_D$ −39° (*c*, 1·2) [Found (after drying at 15°/0·01 mm. for 15 hr.) : C, 75·4; H, 10·5. $C_{29}H_{48}O_4$ requires C, 75·6; H, 10·5%].

(*b*) Methyl 5 : 6β-dihydroxycholestane-3β-carboxylate (3 g.) was oxidised in acetic acid (100 c.c.) with chromium trioxide (420 mg.) in acetic acid (10 c.c.) at 25° for 16 hr. Methanol was then added, the solution diluted with water, and the product isolated in the usual manner. Chromatography of the product on aluminium oxide (90 g.), using benzene (300 c.c.) as eluant, furnished some oily material, whilst use of ether–benzene (1 : 19; 5 × 300 c.c.) gave methyl 5-hydroxy-6-oxocholestan-3β-carboxylate (2·2 g.), which, crystallised from pentane, had m. p. and mixed m. p. with the previous preparation 151—152°.

Cholest-5-ene-3β-carboxylic Acid.—Methyl 5-hydroxy-6-oxocholestane-3β-carboxylate (600 mg.) was refluxed in diethylene glycol (25 c.c.) with potassium hydroxide (800 mg.) and hydrazine hydrate (2 c.c.) for 45 min.; the temperature was allowed to rise to 210° and refluxing continued for 12 hr. Dilution with water, acidification, and ether extraction gave, after the usual washing, drying, and evaporation, a product, which was extracted with pentane to leave cholest-5-ene-3β-carboxylic acid (220 mg.), m. p. and mixed m. p. 215—219°. Esterification (diazomethane) gave methyl cholest-5-ene-3β-carboxylate, m. p. and mixed m. p. 101° (from methanol).

Anhydride of 5-Hydroxy-6-oxocholestane-3β-carboxylic Acid and Acetic Acid.—5-Hydroxy-6-oxocholestane-3β-carboxylic acid (200 mg.) was refluxed in acetic anhydride (12 c.c.) for 45 min., solvent was removed under reduced pressure, and the mixed *anhydride* of 5-hydroxy-6-oxocholestane-3β-carboxylic and acetic acid was obtained by crystallisation from ethyl acetate; it had m. p. 209—211°, $[\alpha]_D$ −37° (*c*, 0·8) [Found (after drying at 80°/0·001 mm. for 5 hr.) : C, 74·2; H, 10·4. $C_{30}H_{48}O_5$ requires C, 73·7; H, 9·9%]. Hydrolysis of the anhydride with methanolic N-potassium hydroxide regenerated the original acid.

The infra-red absorption spectra were determined by courtesy of Dr. R. Norman Jones in the Ottawa Laboratories of the National Research Council of Canada by one of us (G. R.); we thank Dr. Page of Glaxo Laboratories Ltd. for confirmation of our interpretation of the curves. Two of us (G. R.; R. J. S.) gratefully acknowledge the financial support of the Department of Scientific and Industrial Research.

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Phase Relationships in the Pyridine Series. Part IV. The Miscibility of the Ethylpyridines and Dimethylpyridines with Water.*

By J. D. Cox.

[Reprint Order No. 5161.]

The miscibility with water of 2-, 3-, and 4-ethylpyridine and of 2 : 3-, 3 : 4-, and 3 : 5-dimethylpyridine is examined. All six compounds are partially miscible with water and give rise to solubility curves of the closed-loop type; the lower consolute point of the 3-ethylpyridine–water system could not, however, be reached owing to separation of a solid phase. The relation between solubility in water and molecular structure in the pyridine series is discussed.

IN Part I (Andon and Cox, *J.*, 1952, 4601) the solubilities in water of the three methylpyridines and of 2 : 4-, 2 : 5-, and 2 : 6-dimethylpyridine were reported. These dimethylpyridines were shown to belong to the comparatively rare group of compounds which form mixtures with water having both upper and lower consolute temperatures. The present paper deals with the solubility in water of the three ethylpyridines and of the three dimethylpyridines which were not studied previously.

EXPERIMENTAL

Materials.—As in previous work in this series, considerable care was taken to secure the compounds in an adequate state of purity. As far as is known, the compounds used were free

* The paper entitled " The thermodynamic properties of dilute solutions of pyridine bases in water " (Andon, Cox, and Herington, *Discuss. Faraday Soc.*, 1953, **15**, 168) is regarded as Part III. Part II, *J.*, 1952, 4606.

from contaminants which were themselves much less soluble (*e.g.*, hydrocarbons) or much more soluble (*e.g.*, ammonia) in water. The amount of water present in each sample (*ca.* 0·05% by wt.) was measured by infra-red spectroscopy (Coulson, Hales, and Herington, *J.*, 1951, 2125) and due allowance made, where necessary, in calculating the compositions of the mixtures.

2-*Ethylpyridine*.—A sample, prepared by selective hydrogenation of technical-grade 2-vinylpyridine and purified by fractional distillation, had b. p. 144·5—144·8°/700 mm. No impurity, apart from water, was disclosed by infra-red spectroscopy.

3-*Ethylpyridine*.—Nicotinic acid of high purity was converted into methyl 3-pyridyl ketone hydrochloride by Strong and McElvain's method (*J. Amer. Chem. Soc.*, 1933, **55**, 816), and the ketone was reduced to 3-ethylpyridine by that of Fand and Lutomski (*ibid.*, 1949, **71**, 2931). The crude product was fractionally distilled in a Podbielniak microdistillation column (equivalent to about 30 theoretical plates) to give a main fraction, b. p. 166°/760 mm. The presence of an unidentified impurity was indicated by the infra-red spectrum, although the ultra-violet spectrum agreed well with that published (Coulson, Hales, Holt, and Ditcham, *J. Appl. Chem.*, 1952, **2**, 71). Ketones appeared to be absent.

FIG. 1. *Solubility curves for the systems* (a) *2-ethylpyridine–water and* (b) 2 : 3-*dimethylpyridine–water.*

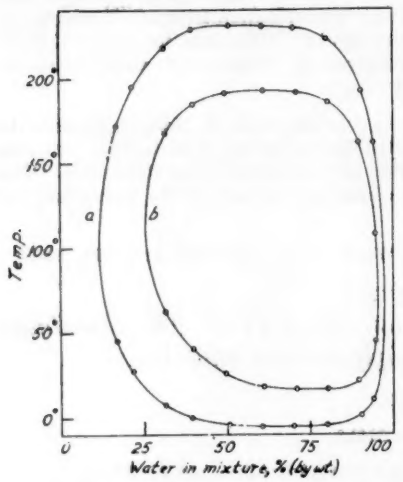
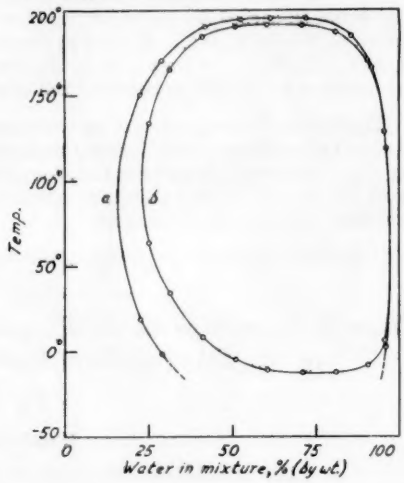


FIG. 2. *Solubility curves for the systems* (a) *3-ethylpyridine–water and* (b) 3 : 5-*dimethylpyridine–water.*



4-*Ethylpyridine*.—A sample, prepared by Frank and Smith's method (*Org. Synth.*, 1947, **27**, 38) and purified by fractional distillation, had b. p. 165—165·5°/760 mm. The infra-red spectrum disclosed the presence of impurities, but these did not exceed 1% by weight.

2 : 3-*Dimethylpyridine*.—A sample of this base, purchased from Kodak Ltd., was purified by a combination of fractional distillation and fractional freezing. The sample used contained *ca.* 0·2% of 2 : 4-dimethylpyridine and 0·04% of water, as measured by the infra-red spectrum, but no other impurities could be detected.

3 : 4-*Dimethylpyridine*.—A specimen prepared by Wibaut and Kooyman's method (*Rec. Trav. chim.*, 1944, **63**, 231) and purified by fractional distillation in a Podbielniak microdistillation column had b. p. 111°/98 mm. and appeared from the infra-red spectrum to be of high purity.

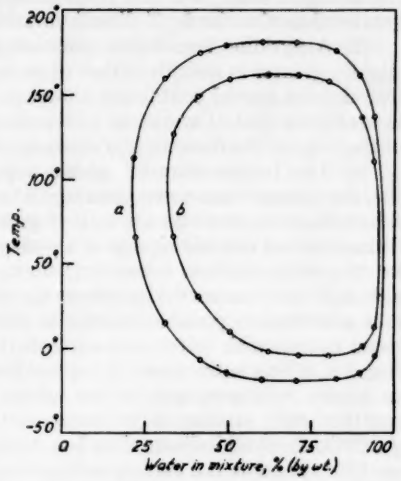
3 : 5-*Dimethylpyridine*.—A sample of this base, kindly supplied by Messrs. Robinson Brothers, West Bromwich, was purified by fractional distillation and fractional freezing. The sample used had b. p. 172·2—172·8°/762 mm. As several bands due to impurity were detected in the infra-red spectrum, the sample was examined by the freezing-point technique (Herington and Handley, *J.*, 1950, 199) and found to be 99·2 mole-% pure.

Solubility Measurements.—As in Part I (*loc. cit.*) Alexejeff's method was employed. Solution temperatures above room temperature were determined with the aid of an electrically-heated metal block; the sealed tube containing the specimen was fixed in a cavity in the middle of the

block and could be viewed through windows, of Chance O.N.20 glass, fixed in the side of the block. Mixing of the liquid layers was effected by rotating the block and hence the specimen through an angle of 180° in a vertical plane.

Solution temperatures below room temperature were determined by the following simple technique. The tube containing the specimen was fixed in a bracket which was then lowered into an unsilvered Dewar vessel filled with methanol; manual shaking of the tube-holder gave adequate mixing of both the methanol and the contents of the tube. The temperature of the bath was lowered by addition of solid carbon dioxide until the lower solution temperature had been passed; the temperature of the bath was then allowed to rise at the rate of 0·1° per min., small pieces of solid carbon dioxide being added when necessary, until the cloud point had been reached.

FIG. 3. *Solubility curves for the systems* (a) *4-ethylpyridine–water and* (b) *3 : 4-dimethylpyridine–water.*



The results of the solubility measurements are shown in Fig. 1, 2, and 3; the solubility–temperature relations in five of the six systems studied may be represented by closed-loop curves. In the 3-ethylpyridine–water system [curve (*a*), Fig. 2] only an upper consolute temperature was found; at every attempt to reach the lower consolute point, a solid phase separated before the two liquid phases had become completely miscible. A tendency to solidify also occurred with mixtures of 4-ethylpyridine and of 3 : 5-dimethylpyridine with water but it was possible to supercool these mixtures, so that the lower solution temperatures could be reached before the onset of freezing. In these two systems, the liquid mixtures at the lower consolute points were thus metastable with respect to a solid phase.

Discussion

Critical solution data for all the nine C_7H_9N alkylpyridines are set out in the Table, the data for 2 : 4-, 2 : 5-, and 2 : 6-dimethylpyridine being taken from Part I (*loc. cit.*).

For a discussion of the relation between solubility and structure, it is convenient to divide these nine isomeric bases into the following groups: (i) those with an α-methyl

Critical solution data for nine alkylpyridine–water systems.

Alkylpyridine	Lower consolute point: Temp.	H_2O, % by wt.†	Upper consolute point: Temp.	H_2O, % by wt.†
2 : 3-Dimethylpyridine	16·5° ± 0·2° *	74	192·6° ± 0·4° *	61·5
2 : 4- ,, ...	23·4 ± 0·2	74·5	188·7 ± 0·3	63
2 : 5- ,, ...	13·1 ± 0·2	73	206·9 ± 0·5	62
2 : 6- ,, ...	34·0 ± 0·2	70	230·7 ± 1	59
3 : 4- ,, ...	− 3·6 ± 0·3	75·5	162·5 ± 0·3	64
3 : 5- ,, ...	−12·5 ± 0·4	74·5	192·0 ± 0·4	63
2-Ethylpyridine	− 5·0 ± 0·3	66	231·4 ± 1	58
3- ,, ...	−35 ± 3 (estimated)		195·6 ± 0·5	63
4- ,, ...	−19·0 ± 0·4	72	181·8 ± 0·3	63·5

* These standard deviations were calculated as described in Part I (*loc. cit.*). No allowance has been made for impurities, because it is impossible to calculate their effects on the solution temperatures. It is believed, however, that such effects are absent in the results reported for 2 : 4-, 2 : 5-, and 2 : 6-dimethylpyridine, as very pure samples of these bases were available. † All ±1%.

group, *viz.*, 2 : 3-, 2 : 4, 2 : 5-, and 2 : 6-dimethylpyridine; (ii) those with a β-methyl group, *viz.*, 2 : 3-, 2 : 5-, 3 : 4-, and 3 : 5-dimethylpyridine; (iii) those with a γ-methyl group, *viz.*, 2 : 4- and 3 : 4-dimethylpyridine; (iv) those with an ethyl group, *viz.*, 2-, 3-, and

4-ethylpyridine. From examination of Figs. 1—3, and of the data of the Table, the following conclusions can be drawn.

(1) The area within the solubility loop of an ethylpyridine–water system is greater than that of a comparable dimethylpyridine–water system (" comparable " here means that the two methyl groups occupy positions in the pyridine ring which are the same distance from the nitrogen atom as is the ethyl group), *e.g.*, the area of the loop for 3-ethylpyridine is greater than that for 3 : 5′-dimethylpyridine (see Fig. 2).

(2) A pyridine homologue containing an α-alkyl group gives rise to a solubility loop slightly greater in area than that of an isomer of the same class [*i.e.*, classes (i), (ii), (iii), or (iv), defined above] containing a β-alkyl group, which, in turn, gives rise to a loop greater in area than that of an isomer of the same class containing a γ-alkyl group; *e.g.*, the areas of the loops of the dimethylpyridines of class (i) lie in the order: $2:6 > 2:5 > 2:3 > 2:4$.

(3) The temperature at which a pyridine homologue is least miscible with water (*i.e.* the temperature corresponding to the widest tie-line of a solubility curve) is higher for a homologue containing an α-alkyl group than it is for an isomer of the same class (as defined above) containing a β- or a γ-alkyl group; *e.g.*, the temperatures of least miscibility for the ethylpyridines [class (iv)] lie in the order: $2 > 3 = 4$. It is noteworthy that, although the monomethylpyridines are completely miscible with water at all temperatures, it is nevertheless possible to infer at what temperature there is a least *tendency* for these bases to mix with water, and as with the dimethylpyridines and the ethylpyridines, it is found that this temperature is highest for the α-isomer. Thus, observations of opalescence in binary mixtures and of the phase relations in ternary mixtures (Part I, *loc. cit.*) together with studies of mixtures of the methylpyridines with deuterium oxide (Cox, *J.*, 1952, 4606) all indicate that 2-methylpyridine has a least tendency to mix with water at *ca.* 110°, whereas the corresponding temperatures for 3-methylpyridine and for 4-methylpyridine are *ca.* 80° and 90°, respectively.

It is of interest to speculate on the reasons underlying these correlations between structure and solubility. By analogy with the benzene series it might be expected that groups *ortho* to the nitrogen atom of the pyridine ring (*i.e.*, in positions 2 or 6) would give rise to a " proximity effect " (Hammett, " Physical Organic Chemistry," McGraw-Hill, New York, 1940, pp. 204—207), so for the moment the discussion will be confined to β- and γ-substituted pyridines. Now the molecule of a pyridine base may be considered to be made up of two parts. The first, the =N-function, is a hydrophilic group and confers solubility in water, but the second, the remaining hydrocarbon part of the molecule, is hydrophobic in nature and gives rise to very low solubility in water. These two effects are, of course, mutually opposed and the observed solubility of a pyridine base is a resultant of the two. When one of the hydrogen atoms of the pyridine ring is substituted by an alkyl group, the hydrocarbon character of the molecule will obviously be increased and in consequence a diminution of solubility will be observed; at the same time, an increase in the electron density in the neighbourhood of the nitrogen atom will take place and this effect will in general be greater for substitition in the 4- than in the 3- or 5-position. (This statement is based on unpublished measurements made in this Laboratory of the dissociation constants of a number of pyridine bases.) If hydrogen-bonding is mainly electrostatic in origin (cf. Davies, *Ann. Reports*, 1946, **43**, 5), it would be expected that an increase in the electron density at the nitrogen atom would lead to more extensive hydrogen-bonding. It would be expected therefore that the greater basicity of γ- as compared with isomeric β-alkylpyridines would give rise to a relatively greater hydrophilic effect and, in consequence, a greater solubility in water. Reference to conclusion (2) above will show that this expectation is in fact borne out. If an ethylpyridine is now considered vis-à-vis a " comparable " dimethylpyridine [see conclusion (1)] it is possible to see how the greater solubility of the dimethylpyridine can arise. The hydrophobic effects in the two molecules will be about the same, but because an ethylpyridine is a much weaker base than a comparable dimethylpyridine, the hydrophilic effect in the latter should be greater, leading to the greater solubility observed. With regard to α-substituted pyridines, it would seem that at low temperatures they are more extensively hydrogen-bonded than isomeric γ-substituted pyridines [cf. conclusion (3) and Part V, succeeding paper] even

though the base strengths of isomeric α- and γ-alkylpyridines are about the same; alternatively, the nitrogen atom in α-alkylpyridines may influence the interaction of the adjacent alkyl group with water. Further study may reveal that very bulky substituents in the 2- or 6-positions tend to reduce, by steric hindrance of the nitrogen atom, the apparently extensive hydrogen-bonding brought about by the presence of methyl or ethyl groups in these positions (cf. Brown and Kanner, *J. Amer. Chem. Soc.*, 1953, **75**, 3865).

It may be readily seen that the solubility curves of the nine systems discussed above have a number of features in common. For example, they all have relatively flat sections at the top and bottom and almost vertical sections near to the " 100% water " ordinate, while the consolute compositions are all of the same order—*ca.* 73% of water by weight (0·94 mole-fraction) at the lower consolute point and *ca.* 64% of water by weight (0·91 mole-fraction) at the upper consolute point. By comparison with the closed-loop systems described by earlier workers (Flaschner, *Z. physikal. Chem.*, 1908, **62**, 493; *J.*, 1909, **95**, 668; Flaschner and McEwen, *J.*, 1908, **93**, 1000; Hudson, *Z. physikal. Chem.*, 1904, **47**, 113; Rothmund, *ibid.*, 1898, **26**, 433; Cox and Cretcher, *J. Amer. Chem. Soc.*, 1926, **48**, 451; Cox, Nelson, and Cretcher, *ibid.*, 1927, **49**, 1080) it is found that the features noted above as being characteristic of pyridine base–water mixtures are in fact common to all systems having closed-loop solubility curves which have so far been described. Of particular interest is the fact that the lower consolute compositions of all these systems are of the order 0·9 mole-fraction of water. Those recent theories which assume the lower consolute composition to be 0·5 mole fraction (Bellemans, *J. Chem. Phys.*, 1953, **21**, 368, 369; Barker and Fock, *Discuss. Faraday Soc.*, 1953, **15**, 188) therefore need modification before direct comparisons can be made between theory and experiment. It also follows that none of the known systems having lower consolute points obeys the equation $G^E = k_T x_2(1 - x_2)$, where G^E is the excess free energy of mixing, k_T is a constant for a given temperature, and x_2 is the mole-fraction of water in the mixture. This is because the above equation requires that $x_2 = 0{\cdot}5$ at the lower consolute temperature. A similar conclusion has already been reached by Herington, using an entirely different argument (*Discuss. Faraday Soc.*, 1953, **15**, 273).

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Phase Relationships in the Pyridine Series. Part V. The Thermodynamic Properties of Dilute Solutions of Pyridine Bases in Water at 25° and 40°.*

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[Reprint Order No. 5162.]

Some thermodynamic properties of very dilute aqueous solutions of methyl- and ethyl-pyridines and of pyridine itself (solutions containing *ca.* 4×10^{-5} mole-fraction of base) have been measured at 25° and 40° by a transpiration technique.

The logarithms of the activity coefficients of the pyridine base components, at a given temperature, have been found to be additive functions of the groups making up the base molecule, so that the activity coefficients of many higher *n*-alkylpyridines can be predicted from the experimental data here presented. The activity coefficients at infinite dilution for nine of the bases at their respective lower consolute temperatures are the same, and by utilizing this fact, together with the above additivity rule, it is demonstrated that the lower consolute temperatures of many higher *n*-alkylpyridines can be calculated. By an examination of the excess partial molar functions and "hydration" functions, it is shown that pyridine homologues containing α-methyl or α-ethyl groups appear to be more extensively hydrogen-bonded with water than their β- or γ-isomers. Finally, the heats of hydration and the entropies of hydration are compared with these functions for other organic solutes. It is concluded that the structures of the aqueous solutions of the pyridine bases at 25° are in no way exceptional and that the closed solubility loops which appear in this series are solely a result of the delicate balance between hydrophobic and hydrophilic groups in the base molecules.

Some measurements of the thermodynamic properties of very dilute solutions of certain pyridine bases in water at 70°, 85°, and 100° were reported in Part III (*Discuss. Faraday Soc.*, 1953, **15**, 168). The present paper gives the results of a similar study of the properties of very dilute aqueous solutions of pyridine, of all the methylpyridines, and of all the pyridine homogues of formula C_7H_9N at 25° and 40°. As explained previously (Part III, *loc. cit.*) it was considered that the investigation of these dilute solutions might yield results which could be interpreted in terms of base–water interactions and in this way information might be obtained on the general conditions necessary for the formation of closed-loop solubility curves.

The equilibrium-still technique described earlier (Part III, *loc. cit.*) did not prove satisfactory at 25° and 40° on account of the low total vapour pressure, so Butler and Shaw's transpiration method (*Proc. Roy. Soc.*, 1930, *A*, **129**, 519), with suitable modification, was employed instead. In every instance the solutions were so dilute (*i.e.*, of the order of 4×10^{-5} mole-fraction) that the measured values of the volatility ratio (α) are indistinguishable from the limiting values at infinite dilution. The volatility ratio is defined in the general case by the equation $\alpha = y_1(1 - x_1)/(1 - y_1)x_1$, where y_1 and x_1 are the mole-fractions of the base in the vapour and liquid respectively. In the present work, however, α may be set equal to y_1/x_1, because y_1 and x_1 are so small that the function $(1 - x_1)/(1 - y_1)$ is very nearly unity.

Experimental

Solutions.—The pyridine bases were drawn from the same sources as those employed in Part I (*J.*, 1952, 4601) and Part IV (*loc. cit.*). Stock base solutions were made up in carbon dioxide-free distilled water to contain *ca.* 4×10^{-5} mole-fraction of base.

Apparatus.—Fig. 1 shows the essential features of the apparatus. Dry, carbon dioxide-free,

* Part IV, preceding paper.

nitrogen from a cylinder entered the apparatus at *A* and bubbled through a base solution in the saturator unit *B*, which consisted of three tubes inclined to the horizontal as in Butler and Shaw's design (*loc. cit.*); *B* was charged with a stock solution of base through the port *F*. The rate of flow of nitrogen could be accurately controlled by a two-stage reduction valve fitted with a needle valve, and the rate was measured by a flow-meter. The gas was preheated to the temperature of the solution in the saturator *B* by passage through a coil of lead tubing immersed in the thermostatically-controlled tank *E*. The gas stream, after leaving the saturator, passed through two bubblers in series, then out of the apparatus at *D*. A constriction with a spherically-ground seating *C*, into which fitted a stainless steel ball-bearing, was situated between the saturator and the bubblers; the ball could be lifted magnetically and transferred to a small side limb, when necessary. The lower parts of the bubblers, which contained 0·1N-sulphuric acid to absorb the bases, were attached by standard taper joints as shown. The whole unit was placed in tank *E*. The gas stream from *D* passed into an aspirator equipped with means for controlling the rate of outflow of water. This device consisted of a long steel rod which fitted, with a small clearance, into a length of capillary tube *G*; the rod could be raised or lowered by means of a screw thread. Experiments were carried out in the following manner. First, the saturator unit and the absorbers were charged with the appropriate solutions and, with the ball valve *C* closed, the apparatus was lowered into tank *E*, and left for 1 hr.; then the

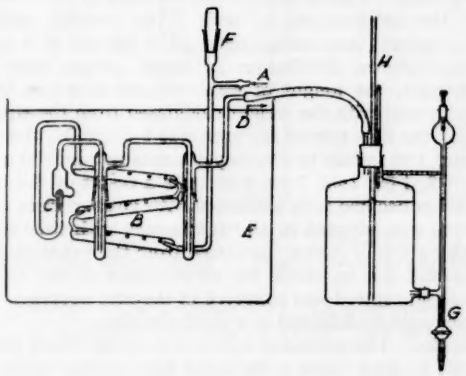


FIG. 1. *Transpiration apparatus.*

aspirator, which was filled with water, was connected to *D* by rubber tubing and, with ball-valve *C* now open, a slow stream of nitrogen was passed through the apparatus. The tap of the aspirator was opened, and the outflowing water was collected in a measuring cylinder; the position of the rod in capillary *G* was regulated so that the water level in the barometer tube *H* remained as close as possible to the level in the aspirator. At the end of an experiment, these two water levels were made to coincide and the nitrogen stream was stopped. Ball-valve *C* was shut, the transpiration unit was removed from the bath, and the contents of the bubblers were analyzed as described below. The volume of water removed from the aspirator (*V* l.) and the temperature of the water and of the gas in the aspirator were recorded. The barometric pressure (P_a, mm. Hg) was measured.

Analysis and Calculation.—The contents of the absorbers were transferred to volumetric flasks and made up to standard volumes with 0·1N-sulphuric acid. The resulting solutions were analyzed for their pyridine base content by ultra-violet spectroscopy. Aliquot portions of the original base solutions, after appropriate dilution with 0·1N-sulphuric acid, were analyzed in like manner. It should be noted that the amounts of base removed by transpiration never exceeded 0·5% of the amounts originally present in the stock solutions; it was therefore justifiable to consider the concentration of base in the saturator to be the same at the end of an experiment as at the beginning. Measurements of optical density were made by means of a Unicam SP 500 Spectrophotometer at five convenient wave-lengths (usually at $\lambda_{max.}$, $\lambda_{max.} - 4$, $\lambda_{max.} - 2$, $\lambda_{max.} + 2$, and $\lambda_{max.} + 4$, mμ).

Now let the optical density of the original solution of the base, after having been diluted *l* times, be *m*, and let the optical density (at the same wave-length) of the solution prepared from the absorbing solutions be *n*. Suppose, further, that the vapour removed by transpiration

from the base stock solution would have had a volume q ml. if it had been condensed and that the absorbing solution has been made up to r ml. Then $\alpha = nr/lmq$ and the only quantity on the right-hand side of this equation which is not immediately known is q; this may be calculated as follows.

Since in the present experiments the vapour always consisted predominantly of water (*i.e.*, the vapour contained more than 99·9% of water by weight) the condensed liquid from the vapour could be assumed to have the same density as water. This density was taken as unity for the present purposes. The volume, in c.c., of the vapour (corrected to that of a gas under 760 mm. pressure at 0° c) removed by transpiration is therefore $22{,}400q/18$ if it is assumed that the vapour behaves as an ideal gas. It can then be shown, by using Dalton's law, that:

$$q = [18 \times 273p_2V(P_a - p_3]/[22{\cdot}4 \times 760T_1(P_a - p_2)]$$

where p_3 is the partial pressure of the water vapour within the aspirator and p_2 is the partial pressure of water vapour at the temperature of the saturator; T_1 is the temperature of the gas within the aspirator; V and P_a have been defined on p. 3189.

The effectiveness of the saturator was tested in a series of subsidiary experiments in which it was filled with distilled water while the absorbers were left empty. The gas stream after leaving D (Fig. 1) was led through a trap, cooled at −78°, which was placed between D and the aspirator; a glass connection between D and the trap was electrically heated to a little above the temperature of bath E to prevent condensation of vapour. A transpiration experiment was then carried out, and at the end of it, the condensate in the trap was transferred by high-vacuum distillation at room temperature into a trap, previously weighed; in this manner, the weight of water vapour removed by transpiration could be found directly and compared with the weight calculated from the equation given above. In two experiments in which the flow rate of nitrogen was 8 c.c./min., the ratios of found to calculated weight were 0·99 and 1·00, while in five experiments in which the rate of flow was 15 c.c./min., the ratios were 0·98, 1·00, 1·03, 1·04, 0·99. As a result of these experiments it was concluded that the gas stream became fully saturated with vapour when passed through B at 15 c.c./min., and this flow rate was adopted in all experiments with base solutions; in these latter experiments the quantity q was of course calculated from the equation given. One final preliminary experiment was carried out to check the effectiveness of the two absorbers. It was found that 96% of the base transpired was collected in the first absorber and the remaining 4% in the second, *i.e.*, no base could be detected in a third absorber.

Results.—The measured values of α for the dilute pyridine base solutions studied are recorded in Table 1; each value is the mean from at least three experiments. Also shown are the corresponding values of the activity coefficients of the base components, γ_1, calculated by the relation $\gamma_1 = Py_1/p_1x_1$, where P is the total vapour pressure of the base–water mixture and p_1 is the vapour pressure of the pure base, *i.e.*, the activity coefficients were calculated with reference to the pure liquid bases (at the same temperature) as the standard state. With very dilute solutions, P is indistinguishable from the vapour pressure of water at the temperature being studied, p_2, and since $\alpha = y_1/x_1$ (see above), we may write $\gamma_1 = \alpha p_2/p_1$. Values of p_2 were taken from the tables of Osborne and Meyers (*J. Res. Nat. Bur. Stand.*, 1934, **13**, 1), and wherever possible values of p_1 were calculated by use of the constants of the Antoine equations given by Herington and Martin (*Trans. Faraday Soc.*, 1953, **49**, 154). A direct comparison of calculated and observed values for the vapour pressures of certain of the bases near 25° could be made by use of the experimental measurements by Brown and Barbaras (*J. Amer. Chem. Soc.*, 1947, **69**, 1137). The relevant values are as follows: at 20°, pyridine 15·82 mm. (obs.) and 15·74 mm. (calc.), 3-methylpyridine 4·46 mm. (obs.) and 4·36 mm. (calc.), and 4-methylpyridine 4·29 mm. (obs.) and 4·15 mm. (calc.); at 20·3°, 2-methylpyridine, 8·55 mm. (obs.) and 8·49 mm. (calc.). The vapour pressures of the seven bases used in this work for which no vapour-pressure data exist, other than the normal b. p.s, were calculated by an empirical method. Use was made of Herington and Martin's observation (*loc. cit.*) that when the values of Antoine's constant B for six bases are plotted against the normal b. p.s a smooth curve is obtained. Hence by interpolation, or extrapolation, it was possible to deduce the Antoine constants B of the seven bases whose vapour pressures were required, since their normal b. p.s were known (Eguchi, *Bull. Chem. Soc. Japan*, 1928, **3**, 227; and Part IV, preceding paper). Examination of the published values showed that the Antoine constant C is close to 210 for the three monomethylpyridines and close to 208 for the two dimethylpyridines studied by Herington and Martin, so it was assumed that $C = 208$ for the seven bases in question. The Antoine constants A of these seven

bases were then found by setting t in the Antoine equation equal to the b. p. (in °c) at 760 mm. Finally, the constants A, B, and C were used to calculate the vapour pressures, p_1, at 25° and 40° shown in Table 1. The validity of this procedure was tested by comparing the known

TABLE 1. *Volatility ratios, α, and activity coefficients, γ_1, of the pyridine-base components of very dilute aqueous base solutions.*

	t (c)	α	σ_α *	p_1, mm.	γ_1	$\sigma_{\gamma,1}$ †	ln γ_1
Pyridine	25°	15·70	0·20	20·81	17·9	0·2	2·884
	40	17·29	0·08	45·10	21·2	0·1	3·054
2-Methylpyridine	25	17·65	0·10	11·22	37·4	0·2	3·622
	40	21·13	0·14	25·49	45·9	0·3	3·827
3-Methylpyridine	25	13·83	0·05	5·96	55·1	0·2	4·009
	40	16·52	0·11	14·15	64·6	0·4	4·168
4-Methylpyridine	25	10·54	0·15	5·68	44·1	0·6	3·787
	40	12·97	0·10	13·52	53·1	0·4	3·972
2-Ethylpyridine	25	29·21	0·15	4·69	147·9	0·8	4·997
	40	37·00	0·14	11·43	179·1	0·7	5·188
3-Ethylpyridine	25	18·43	0·13	2·19	199·9	1·4	5·298
	40	22·32	0·20	5·60	220·4	2·0	5·396
4-Ethylpyridine	25	14·72	0·17	2·22	157·5	1·8	5·060
	40	17·38	0·14	5·67	169·6	1·4	5·134
2 : 3-Dimethylpyridine	25	12·71	0·17	2·75	109·8	1·5	4·699
	40	16·77	0·07	6·92	134·1	0·6	4·899
2 : 4-Dimethylpyridine	25	11·90	0·13	3·12	90·6	1·0	4·507
	40	16·01	0·15	7·79	113·7	1·1	4·734
2 : 5-Dimethylpyridine	25	15·23	0·11	3·25	111·3	0·8	4·712
	40	20·47	0·14	8·10	139·8	1·0	4·940
2 : 6-Dimethylpyridine	25	18·57	0·14	5·58	79·0	0·6	4·370
	40	25·90	0·13	13·44	106·6	0·5	4·669
3 : 4-Dimethylpyridine	25	6·50	0·03	1·23	125·5	0·6	4·832
	40	8·40	0·03	3·18	146·1	0·5	4·984
3 : 5-Dimethylpyridine	25	12·34	0·08	1·69	173·4	1·1	5·156
	40	15·82	0·11	4·41	198·4	1·4	5·290

* Standard deviations of the mean values of α.

† Standard deviations of the mean values of γ_1 calculated from col. 4. These values of $\sigma_{\gamma,1}$ do not of course take into account possible errors in the estimation of the vapour pressures of the bases.

vapour pressures of two bases with the calculated values, as follows: 2 : 3-dimethylpyridine at 81·2°, 55·8 mm. (obs.), 53·4 mm. (calc.); 3 : 4-dimethylpyridine at 111·0°, 98·3 mm. (obs.), 95·8 mm. (calc.).

DISCUSSION

Table 1 shows that the volatility ratios, α, for all the bases in dilute aqueous solution at 25° and 40° are considerably greater than unity. Since pyridine and 2-, 3-, and 4-methylpyridine are miscible with water in all proportions (Part I, *J.*, 1952, 4601), and since the vapour pressures of the pure bases at a given temperature are less than the vapour pressure of water at that temperature, it follows from the data of Table 1 that the base–water binary systems containing these four bases must all exhibit homogeneous minimum boiling azeotropes at 25° and 40°.

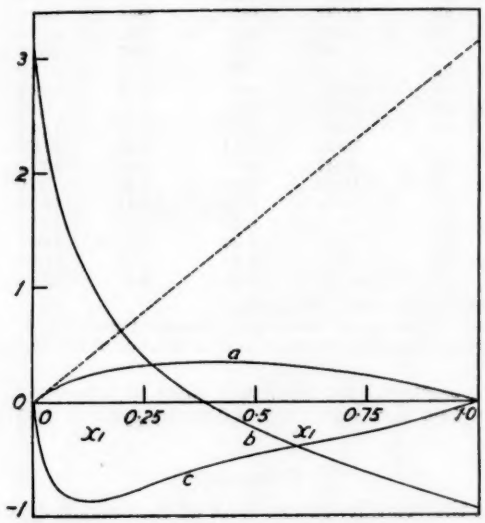
As explained above, the values of ln γ_1 (component 1 being the base) listed in Table 1 refer to very dilute solutions, so that the values will be numerically indistinguishable from those for the infinitely dilute solution. Inspection of Table 1 reveals that the values of ln γ_1 at any temperature are additive functions of the groups within the pyridine base molecule, provided that due regard is paid to the positions of the substituents with respect to the nitrogen atom of the pyridine ring. For example, by combining the results for pyridine with those for the three methylpyridines at 25° it is found that the contributions of the α-, β-, and γ-methyl groups to ln γ_1 are 0·74, 1·12, and 0·90, respectively. By using these figures together with the value of ln γ_1 for pyridine itself it is possible, by assuming additivity, to compute the values of ln γ_1 for all the dimethylpyridines at 25°. Thus the following values were obtained: 2 : 6-dimethylpyridine 4·36; 2 : 3- or 2 : 5-dimethylpyridine 4·74; 2 : 4-dimethylpyridine 4·52; 3 : 5-dimethylpyridine 5·12; 3 : 4-dimethylpyridine 4·90. A very satisfactory measure of agreement is found between these figures and the experimental results for 2 : 6-, 2 : 3- or 2 : 5-, 2 : 4-, 3 : 5-, and 3 : 4-dimethylpyridine,

respectively (Table 1). Analysis of the experimental results for 40° (Table 1) and for pyridine, 2-, 3-, and 4-methylpyridine, and 2 : 5- and 2 : 6-dimethylpyridine in the temperature range 70—100° (Part III, *loc. cit.*) shows that they also obey this additivity rule. There is approximately a constant difference, equal to 1·31 units, between the ln γ_1 values for the ethyl and methyl homologues at 25° (the actual differences are 1·38 units for the α-, 1·29 units for the β-, and 1·27 units for the γ-position) and an average difference of 1·25 units between the same quantities at 40°.

The discovery that ln γ_1 is an additive function enables the values of this quantity for higher *n*-alkylpyridine homologues (*e.g.*, the trimethylpyridines and ethylmethylpyridines) to be calculated, and this also allows an estimate to be made of the solubility properties of these bases.

When the values of ln γ_1 for the 2 : 5- and 2 : 6-dimethylpyridines reported in Table 1 and the values recorded in Table 1 of Part III (*loc. cit.*) were plotted against temperature,

FIG. 2.

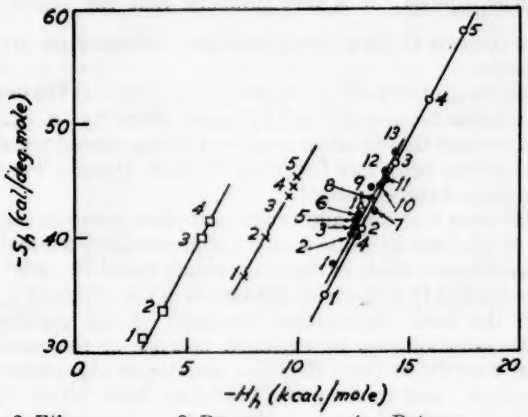


Curve *a* is the plot of G^E/RT against x_1.
Curve *b* is the plot of $[\partial(G^E/RT)/\partial x_1]_T$ against x_1.
Curve *c* is the plot of $x_1(1 - x_1)[\partial^2(G^E/RT)/\partial x_1^2]_T$ against x_1.

it was found that the values of ln γ_1 at the respective lower critical solution temperatures (Part IV, preceding paper) were 4·48 and 4·56, respectively; this treatment was next applied to the results at 25° and at 40° for 2 : 3- and 2 : 4-dimethylpyridine on the assumption that the curves had the same general shapes as those of the 2 : 5- and 2 : 6-isomers. Values of ln γ_1 equal to 4·54 and 4·49 at the lower critical solution temperatures were then obtained for 2 : 3- and 2 : 4-dimethylpyridine respectively. This procedure was also applied to the results for the five other relevant systems listed in Table 1. Here, however, the extrapolations were rather long and in consequence the estimated values of ln γ_1 at the lower critical solution temperatures were less reliable. Nevertheless, the graphs show that these values of ln γ_1 must lie between 4·35 and 4·65. Hence it follows that at the lower consolute temperatures of the nine partially miscible base–water mixtures studied, the values of ln γ_1 are all close to 4·5, *i.e.*, γ_1 is close to 90. If now the very reasonable assumption is made that this relation holds for binary mixtures of higher *n*-alkyl homologues of pyridine with water, it is possible to estimate the lower consolute temperatures by using the data presented in Table 1. Consider for instance 2 : 4 : 6-trimethylpyridine : the values of ln γ_1 over a range of temperatures may readily be calculated

by the additivity rule given above. Extrapolation of the plot of ln γ_1 against temperature to ln $\gamma_1 = 4{\cdot}5$ then shows that the lower consolute temperature of this base with water should be at $+2° \pm 3°$, which is in agreement with Rothmund's measurement, *i.e.*, $+6{\cdot}4°$ (*Z. physikal. Chem.*, 1898, **26**, 433); recent experiments in this laboratory with an authentic sample of 2 : 4 : 6-trimethylpyridine have confirmed Rothmund's result. There is probably very little steric hindrance between the alkyl groups and the nitrogen atom, or between the alkyl groups themselves, in the compounds studied in the present work, because these alkyl groups contained at the most two carbon atoms. If, however, aqueous solutions of pyridine homologues with very bulky substituents (*e.g.*, 2 : 6-di-*tert.*-butylpyridine; cf. Brown and Kanner, *J. Amer. Chem. Soc.*, 1953, **75**, 3865) were studied it is

FIG. 3.



□ 1, Methane. 2, Ethane. 3, Propane. 4, *n*-Butane.
(Calc. from the measurements of Claussen and Polglase, *J. Amer. Chem. Soc.*, 1952, **74**, 4817.)

× 1, Benzene. 2, Toluene. 3, *p*-Xylene. 4, Ethylbenzene. 5, *m*-Xylene.
(Calc. from the measurements of Bohon and Claussen, *ibid.*, 1951, **73**, 1571).

● 1, Pyridine. 2, 4-Ethylpyridine. 3, 3-Methylpyridine.
4, 4-Methylpyridine. 5, 2-Methylpyridine. 6, 3-Ethylpyridine.
7, 3 : 4-Dimethylpyridine. 8, 3 : 5-Dimethylpyridine. 9, 2-Ethylpyridine.
10, 2 : 3-Dimethylpyridine. 11, 2 : 4-Dimethylpyridine. 12, 2 : 5-Dimethylpyridine.
13, 2 : 6-Dimethylpyridine.

○ 1, Methanol. 2, Ethanol. 3, *n*-Propanol. 4, *n*-Butanol. 5, *n*-Pentanol.
(Butler, *Trans. Faraday Soc.*, 1937, **33**, 229.)

△ 1, Ethylamine (*idem, loc. cit.*)

probable that effects due to steric hindrance would appear. Predictions of solubility in such cases should obviously be made with caution.

Further implications of the finding that ln γ_1 equals 4·5 for all the bases at their lower consolute temperatures will now be considered. In Fig. 2, curve *a* is a plot for an imaginary system of G^E/RT against x, where G^E is the molar excess free energy of mixing. It follows from the properties of partial molar quantities that the tangent to this curve at $x_1 = 0$ cuts the ordinate $x_1 = 1$ at the point ln γ_∞. (As explained above, the values of γ_1 reported in the present paper will be indistinguishable from values at infinite dilution, *i.e.*, γ_∞.) Curve *b* is a plot of $[\partial(G^E/RT)/\partial x_1]_T$ against x_1, and curve *c* is the plot of the function $x_1(1 - x_1)[\partial(^2G^E/RT)/\partial x_1{}^2]_T$ against x_1. Since for any binary system $[\partial(G^E/RT)\partial x_1]_T$ is equal to ln (γ_1/γ_2), it follows that curve *b* is also a plot of ln (γ_1/γ_2) against x_1, and curve *c* is also a plot of $x_1(1 - x_1)[\partial(\ln \gamma_1/\gamma_2)/\partial x_1]_T$ against x_1. Now it can be shown that at a consolute temperature, either upper or lower, the function $x_1(1 - x_1)[\partial^2(G^E/RT)/\partial x_1{}^2]_T$ equals -1 (see, *e.g.*, Prigogine and Defay, " Thermodynamique chimique," Desoer, Liége,

1950), *i.e.*, the consolute temperature is the temperature at which the minimum of curve *c* lies at −1. Reference to Part IV (preceding paper) will show that the lower consolute compositions, expressed as the mole-fraction of base, of the partially miscible pyridine base–water mixtures studied, lie between 0·06 and 0·08. The *c* curves of all these systems at their consolute temperatures must therefore have minima at $x_1 \simeq 0{\cdot}07$; moreover, because of the functional relationship between the *c* and *b* curves it follows that the *b* curves must all have identical slopes at $x_1 \simeq 0{\cdot}07$.

Further, the limiting value of $\ln(\gamma_1/\gamma_2)$ as x_1 approaches zero (*i.e.*, $\ln \gamma_\infty$) is approximately 4·5 for each of the nine systems at their lower consolute temperatures, so it is almost certain that the *b* curves of these systems at their lower consolute temperatures will prove to be identical over the composition range $x_1 = 0$ to $x_1 = 0{\cdot}07$. Also, because $G^E/\boldsymbol{R}T$ equals $\int_0^{x_1} \ln(\gamma_1/\gamma_2) \cdot dx_1$, it is very probable that the curves of $G^E/\boldsymbol{R}T$ plotted against x_1 for these systems at their lower consolute temperatures are identical over the same composition range.

Since for the systems studied here, $\gamma_\infty = 90$ and $x_1 = 0{\cdot}07$ at the lower consolute point it follows that the relation between G^E and x_1 is not given by an equation of the form $G^E = k_T x_1(1 - x_1)$ because this equation requires that γ_∞ should equal 7·4 and x_1 should equal 0·50 at the consolute point (see Copp and Everett, *Discuss. Faraday Soc.*, 1953, **15**, 174, 268, for a discussion of this equation).

The results at 25° show that each additional methylene group increases the value of the activity coefficient of the base in dilute solution approximately 2·5-fold, as had previously been found for measurements made in the temperature range 70—100° (Part III, *loc. cit.*). In Part III it was remarked that the finer differences in the values of γ_∞ for isomers could be correlated with the basic dissociation constants of the pyridine homologues. If consideration of the α-homologues be excluded because of the possibility of an *ortho*-proximity effect (cf. Part IV, *loc. cit.*) then this correlation also exists at 25° in the sense that 3-methyl-, 3-ethyl-, and 3 : 5-dimethyl-pyridine have larger values of γ_∞ than, respectively, 4-methyl-, 4-ethyl-, and 3 : 4-dimethyl-pyridine. Unpublished results from this laboratory show that the dissociation constants can be arranged in the following order: 3-methyl- < 4-methyl-; 3-ethyl- < 4-ethyl-; 3 : 5-dimethyl- < 3 : 4-dimethyl-pyridine.

Two sets of thermodynamic functions were calculated from the results given in Table 1, namely, the excess partial molar functions and the "hydration" functions (Butler, "Chemical Thermodynamics," Macmillan, London, 1946, p. 389). The limiting values of the partial molar excess free energies of the base compounds ($\bar{G}^E_\infty$) were calculated by means of the equation $\bar{G}^E_\infty = \boldsymbol{R}T \ln \gamma_\infty$ (note that γ_∞ equals γ_1 in the present experiments) and the corresponding partial molar excess entropies ($\bar{S}^E_\infty$) and partial molar heats of mixing ($\bar{H}^M_\infty$) were calculated in the usual way from the equations $-\bar{S}^E_\infty = (\partial \bar{G}^E_\infty/\partial T)_p$ and $\bar{H}^M_\infty = \bar{G}^E_\infty - T(\partial \bar{G}^E_\infty/\partial T)_p$.

The free energy of hydration (G_h) was calculated from the expression $G_h = \boldsymbol{R}T \ln \alpha p_2$. This free energy is the difference between the partial molar free energies of the base in two standard states. The initial state is that of a gas at 1 atm. pressure at the prevailing temperature, and the final state is a hypothetical one in which the mole-fraction of the base is unity but where certain thermodynamic properties are those of an infinitely dilute solution. The entropies (S_h) and enthalpies (H_h) of hydration were calculated by the usual equations $-S_h = (\partial G_h/\partial T)_p$ and $H_h = G_h - T(\partial G_h/\partial T)_p$.

In the evaluation of the expressions $(\partial \bar{G}^E_\infty/\partial T)_p$ and $(\partial G_h/\partial T)_p$ it was assumed that $\bar{G}^E_\infty$ and G_h both varied linearly with T over the temperature range 25—40°. Similar assumptions have invariably been made by other workers but it follows from the existence of closed solubility loops in the systems studied here that $\bar{S}^E_\infty$ (and hence S_h) must vary with temperature; $\bar{G}^E_\infty$ and G_h cannot, therefore, be true linear functions of T. Nevertheless, very little error in the estimations of $\bar{S}^E_\infty$, S_h, $\bar{H}^M_\infty$, and H_h will arise by assuming for the present systems that the plots of $\bar{G}^E_\infty$ (or G_h) against T are linear over a range as short as

15°. The values of the functions so found are listed in Table 2. The only previously published value for any of the data of Table 2 is a calorimetric value of $\bar{H}^{M}_{\infty}$ (−2·27 kcal./mole) for pyridine (Baud, *Bull. Soc. chim.*, 1909, **5**, 1022), which may be compared with the value −2·0 kcal./mole reported in the Table.

TABLE 2. *Thermodynamic functions for some very dilute aqueous solutions, at* 25°.

Solute	$\bar{G}^{E}_{\infty}$ (kcal./mole)	$-\bar{S}^{E}_{\infty}$ (cal./deg. mole)	$-\bar{H}^{M}_{\infty}$ (kcal./mole)	G_h (kcal./mole)	$-S_h$ (cal./deg. mole)	$-H_h$ (kcal./mole)
Pyridine	1·709 ± 0·008 *	12·4 ± 0·5 *	2·00 ± 0·17 *	−0·423 †	37·6 †	11·65 †
2-Methylpyridine	2·145 ± 0·004	15·3 ± 0·4	2·42 ± 0·11	−0·355	41·2	12·64
3-Methylpyridine	2·374 ± 0·003	14·2 ± 0·3	1·87 ± 0·10	−0·498	40·6	12·60
4-Methylpyridine	2·243 ± 0·008	14·9 ± 0·6	2·19 ± 0·19	−0·659	40·8	12·82
2-Ethylpyridine	2·960 ± 0·003	17·5 ± 0·2	2·26 ± 0·06	−0·057	44·4	13·31
3-Ethylpyridine	3·138 ± 0·004	14·4 ± 0·5	1·15 ± 0·13	−0·328	41·8	12·78
4-Ethylpyridine	2·997 ± 0·007	13·0 ± 0·6	0·86 ± 0·17	−0·462	40·3	12·48
2 : 3-Dimethylpyridine	2·783 ± 0·008	17·2 ± 0·5	2·35 ± 0·16	−0·549	44·4	13·79
2 : 4-Dimethylpyridine	2·669 ± 0·007	17·9 ± 0·6	2·67 ± 0·17	−0·587	45·0	14·02
2 : 5-Dimethylpyridine	2·791 ± 0·004	18·4 ± 0·4	2·68 ± 0·12	−0·441	45·5	14·00
2 : 6-Dimethylpyridine	2·588 ± 0·005	20·5 ± 0·4	3·53 ± 0·11	−0·325	47·3	14·44
3 : 4-Dimethylpyridine	2·862 ± 0·003	15·6 ± 0·2	1·78 ± 0·07	−0·945	42·2	13·54
3 : 5-Dimethylpyridine	3·054 ± 0·004	15·6 ± 0·4	1·59 ± 0·11	−0·566	43·2	13·45
Benzene ‡	4·616	13·5	−0·59	3·385	36·7	7·56
Toluene ‡	5·337	15·9	−0·60	3·391	40·1	8·55
Ethylbenzene ‡	6·071	19·1	−0·38	3·476	44·6	9·83
m-Xylene ‡	6·112	19·2	−0·40	3·436	44·8	9·92
p-Xylene ‡	6·100	19·0	−0·45	3·456	44·4	9·79

* These standard errors were calculated from the standard errors given in Table 1.

† The standard errors attaching to G_h, $-S_h$, and $-H_h$ are respectively the same as those attaching to $\bar{G}^{E}_{\infty}$, $-\bar{S}^{E}_{\infty}$, and $-\bar{H}^{M}_{\infty}$ for the same solute.

‡ The thermodynamic functions for the aromatic hydrocarbons were calculated from Bohon and Claussen's measurements (*J. Amer. Chem. Soc.*, 1951, **73**, 1571) with the aid of vapour-pressure data calculated from Table 5k of A.P.I.–N.B.S. Project 44.

Inspection of the listed values of $\bar{S}^{E}_{\infty}$ and $\bar{H}^{M}_{\infty}$ for the pyridine series shows that these values are all negative and numerically large. Now the temperature to which these values refer, 25°, is fairly close to the lower consolute points of the dimethylpyridine and ethylpyridine systems with water. It is not surprising therefore that $\bar{S}^{E}_{\infty} < 0$ and $\bar{H}^{M}_{\infty} < 0$ since theory shows that it is necessary that $S^{E} < 0$ and $H^{M} \leqslant 0$ provided the plots of G^{E}, S^{E}, and H^{M} against x_1 maintain the same sign for all values of x_1 (see, *e.g.*, Copp and Everett, *loc. cit.*).

Comparison of the values of $\bar{H}^{M}_{\infty}$ at 25° with similar values at 85° (Part III, *loc. cit.*) shows that in every instance the values change with temperature by 2—3 kcal./mole in the direction indicating a large positive value for $\bar{C}^{E}_{p\infty}$. This is the expected behaviour for systems having closed solubility loops (Copp and Everett, *loc. cit.*).

The data in Table 2 indicate that an alkyl group in the α-position of the pyridine nucleus gives rise to much larger values of $-\bar{S}^{E}_{\infty}$ and $-\bar{H}^{M}_{\infty}$ than does the same group in the β- or γ-positions. Now it is known that the physical properties of the α-alkylpyridines are often very different from those of the isomers containing β- or γ-groups (*e.g.*, the b. p.s of α-, β-, and γ-methylpyridines are respectively 129°, 144°, and 145°), so it might be thought that the " α-effect " apparent in the $-\bar{S}^{E}_{\infty}$ and $-\bar{H}^{M}_{\infty}$ values noted above might be due to the choice of the pure liquid as the standard state. However, an examination of the $-S_h$ and $-H_h$ values of Table 2 shows that the " α-effect " persists even when the vapour at 1 atm. pressure is taken as the standard state. The " α-effect " in the $-S_h$ and $-H_h$ values is not very striking for the monomethylpyridines but can be seen readily in the results for the ethylpyridines and dimethylpyridines. The conclusion would therefore seem to be that the pyridine homologues containing α-methyl or α-ethyl groups are more extensively hydrogen-bonded to water at 25° than their β- or γ-isomers, since large negative excess entropies and negative heats of mixing are well known to result from hydrogen-bonding.

Finally, the properties of dilute aqueous solutions of the pyridine bases are compared

with those of dilute aqueous solutions of other organic compounds, and for this purpose it is convenient to consider the values of $-S_h$ and of $-H_h$. A comparison of the properties of dilute solutions of the aromatic hydrocarbons with those of the pyridine bases is particularly instructive because the benzene series bears such a close structural relationship to the pyridine series. Appropriate values for the aromatic hydrocarbons have been calculated from the measurements of Bohon and Claussen (*J. Amer. Chem. Soc.*, 1951, **73**, 1571) and are set out in Table 2, which shows that, although the $-S_h$ values of analogues in the two series (*e.g.*, pyridine compared with benzene; methylpyridines compared with toluene) are closely similar, yet there is a striking difference in the $-H_h$ values. This marked difference arises chiefly from the fact that the pyridines dissolve in water at 25° with a considerable evolution of heat, owing to formation of hydrogen bonds, whereas the aromatic hydrocarbons dissolve in water at 25° with absorption of heat. Other workers have also observed that molecules of approximately the same size have closely similar values of S_h but may have very different values of H_h; thus Butler and Reid (*J.*, 1936, 1171) found such a relation for ethane, methyl chloride, and methyl alcohol. Butler (*op. cit.*, p. 396) has also drawn attention to the fact that $-S_h$ bears an approximately linear relation to $-H_h$ for solutions of the permanent gases in water and for solutions of the alcohols in water. Examination of the present measurements on the pyridine series shows that the same relation holds, as can be seen from Fig. 3, where $-S_h$ is plotted against $-H_h$ for a number of compounds at 25°. A feature of this diagram which does not seem to have been emphasized before is that it is made up of parallel lines of slope 0·0034 and that each homologous series occupies a separate line. The origin of this behaviour becomes evident if the equation is written as $-S_h = -H_h/T + G_h/T$. Now it happens that in the ascent of all the homologous series which have been studied at 25°, G_h changes very slowly (*ca.* 0·1 kcal. per methylene group) whereas $-H_h$ increases rapidly (*ca.* 1·5 kcal. per methylene group), and therefore to a first approximation G_h/T may be considered as a constant for a given T, so that $-S_h$ varies linearly with $-H_h$, the gradient of the line being equal to $1/T$, *i.e.*, 0·0034 when T equals 298° K.

The plot of $-S_h$ against $-H_h$ for aqueous solutions at 25° is thus made up of a series of parallel straight lines disposed in such a manner that the lines for solutes which are most hydrogen-bonded lie furthest to the right. It may be noted that the line for the pyridine bases at 25° is nearly coincident with that for the aliphatic alcohols; a single point for ethylamine also lies close to the line for the pyridine series. These measurements indicate, therefore, that the structures of aqueous solutions of the pyridines are not in any way exceptional, and it would appear that the reason why these bases form closed solubility loops while the alcohols do not, is to be found in the delicate balance between the hydrophobic and hydrophilic groups within the molecules of the pyridine bases. The result is that any small change in the system, such as that produced by altering the temperature, is sufficient to change markedly the solubility of these bases (cf. Part IV, and Copp and Everett, *locc. cit.*).

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Researches on Acetylenic Compounds. Part XLV. The Alkaline Isomerisation of But-3-ynoic Acid.*

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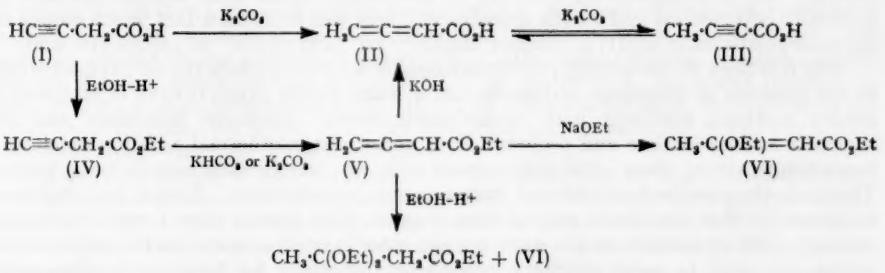
[Reprint Order No. 5303.]

Under alkaline conditions but-3-ynoic acid is isomerised in good yields first to buta-2 : 3-dienoic (allenecarboxylic) acid, then under more vigorous conditions to but-2-ynoic (tetrolic) acid. The properties of buta-2 : 3-dienoic acid and its ester have been examined in some detail.

This communication describes the beginning of an attempt to extend the classical work of Kon and Linstead and their collaborators on the prototropy of ethylenic acids, esters, nitriles, and ketones (see, *inter al.*, Bennett and Baker, *Ann. Reports*, 1931, **28**, 105) to structurally similar substances possessing more than one unit of unsaturation. The obvious starting-point for such a study is the simplest βγ-acetylenic acid (I), which was first prepared by Sargent (Thesis, London, 1948; see Heilbron, Jones, and Sondheimer, *J.*, 1949, 606) by the oxidation of but-3-yn-1-ol with chromic acid. Since then this acid has been obtained by the interaction of propargylmagnesium bromide and carbon dioxide (Wotiz, Matthews, and Lieb, *J. Amer. Chem. Soc.*, 1951, **73**, 5503; cf. Prevost, Gaudemar, and Honigsberg, *Compt. rend.*, 1950, **230**, 1186). The American authors also found that the liquid acidic material obtained from the mother-liquors from (I) had an infra-red absorption spectrum suggesting that the allenic acid (II) was present. By analogy with Wotiz's earlier work on substituted propargyl bromides (*J. Amer. Chem. Soc.*, 1950, **72**, 1639) it was assumed that (II) was formed directly in the Grignard reaction. In view of the method of isolation reported we accept this assumption despite the ready isomerisation of (I) to (II) discussed below.



Preliminary investigations showed that under vigorous alkaline conditions (*e.g.*, 10% sodium hydroxide at 100°) the acid (I) was converted into acetone [presumably *via* (II), or perhaps (III), and acetoacetic acid]. Ethanolic alkali gave β-ethoxycrotonic acid. With milder reagents, however, buta-2 : 3-dienoic acid (II) was obtained. Its strong infra-red absorption band at 1980 cm.$^{-1}$ ($\varepsilon = 140$) made possible a systematic investigation of the effects of varying reaction conditions; optimally, treatment of (I) with 18% potassium carbonate solution at 40° for 3 hr. gave a 92% yield of (II).

Under more vigorous conditions (II) was further isomerised to tetrolic acid (III), a reaction which was studied similarly by using the 2250 cm.$^{-1}$ band ($\varepsilon = 290$) of the acetylenic acid. With 18% potassium carbonate at 90° a yield of 60% was obtained after 6 hours, which sets a limiting value of 1·5 for the equilibrium constant for the anions of (III) and (II). This was determined more accurately by prolonging the reaction period beyond the point of maximal yield of (III); the ratio of the extinction coefficients at the chosen frequencies then became constant, indicating a value for (III)/(II) of 2·22. When the equilibrium was approached from the other side, the value obtained was 2·15. It is

* Part XLIV, *J.*, 1954, 1865.

believed that this result is reliable to about ±0·2 since absorption in this region of the spectrum with appreciable intensity is quite uncommon, and any by-products would presumably be almost transparent.

From the equilibrium constants it follows that the free-energy differences between the anions of (I) and of (II) at 40° is at least 1·5 kcals., and between those of (II) and (III), at 90°, 0·57 kcal. Unfortunately the kinetic distinction between the two isomerisations, and between the second of these and the hydration–decarboxylation reactions which ensue, are insufficient to permit much variation in the reaction conditions for quantitative experiments.

As might have been expected, the ester of (I) isomerised to the allene much more readily than the related anion. Even potassium hydrogen carbonate solution at 50° catalysed the reaction, which with 10% potassium carbonate proceeded almost to completion at 20° in 45 minutes in a heterogeneous system. Dilute ammonia solution effected the same change, though stronger solutions converted the product into β-aminocrotonic ester. Hydrolysis of either ethyl but-3-ynoate (IV) or ethyl buta-2 : 3-dienoate (V) with aqueous sodium hydroxide solution gave the butadienoic acid, together with some β-ethoxycrotonic ester (VI), which is comparatively resistant to hydrolysis. The ethoxy-ester was the main product when either ester was treated briefly with aqueous-ethanolic potassium hydroxide solution; on more prolonged treatment the corresponding acid was, of course, obtained. In contrast to these ready isomerisation reactions under alkaline conditions, (IV) was unaffected by dilute aqueous mineral acids at 20° or even, for brief periods, at 80°.

The allenic acid (II) is lower-melting and more volatile than either of its acetylenic isomers; it is stable in air at room temperature for several weeks. Its ester shows lachrymatory and skin-irritant properties, in contrast to but-3-ynoic and tetrolic esters. The acid can be esterified with diazomethane in low yield only, much polymeric material being formed simultaneously. Ethanolic sulphuric acid esterifies butadienoic acid, but the ester apparently adds ethanol at a comparable rate to give a mixture of β-ethoxycrotonic and ββ-diethoxybutyric ester. When heated in an inert solvent the acid (II) gradually polymerised and a little dehydracetic acid was isolated, a fact which emphasises the close relationship of (II) to diketen, similarly an " anhydride " of acetoacetic acid.

The reactions of the ester (V) with nucleophilic reagents include the addition of ethanol in the presence of potassium carbonate, *i.e.*, a much milder catalyst than is necessary for similar addition reactions with αβ-acetylenic esters. Similarly piperidine and even aromatic amines (aniline and *p*-phenetidine) underwent exothermal addition reactions at room temperature; these latter amines react with, *e.g.*, tetrolic ester only on being warmed. The products were the β-substituted crotonic esters in every case. Thus it is probably safe to generalise that the allenic ester is more reactive than tetrolic ester toward nucleophilic reagents, and equivalent to it; since tetrolic ester is itself a more reactive equivalent of acetoacetic ester in many synthetic procedures (especially for heterocyclic compounds), this may be of some preparative significance.

Perhaps the most remarkable example of the exceptional reactivity to nucleophilic reagents at the β-carbon atom in these allenes was afforded by the action of lithium aluminium hydride on the acid and ester. The primary products were vinylacetic acid and ester, respectively; with an excess of the reagent these underwent some further reduction to but-3-en-1-ol, but buta-2 : 3-dien-1-ol could not be detected. Here this reagent, generally considered specific for the reduction of the $>C{=}O$, as opposed to the $>C{=}C<$, linkage, actually reduces the latter preferentially. In contrast, αβ-acetylenic esters are reduced first to acetylenic primary alcohols (Bates, Jones, and Whiting, *J.*, 1954, 1854). This behaviour of the simplest allenic ester and acid may be compared with the 1 : 4-addition of Grignard reagents to the 2-butyl derivative of (V) (Wotiz and Matthews, *J. Amer. Chem. Soc.*, 1952, **74**, 2559), though the ester of this substituted allenic acid behaved normally with lithium aluminium hydride.

As a complement to the chemical reduction described above, the partial catalytic hydrogenation of butadienoic acid in the presence of 1·5% palladium on calcium carbonate was examined. The product was essentially pure *cis*-crotonic acid, as judged by the almost complete absence of absorption at 690 cm.$^{-1}$, where the *trans*-isomer has an intense

band. A little vinylacetic acid may also have been present. *threo*-αβ-Dibromocrotonic acid was isolated in 70% yield on bromination, as expected. Preferential attack on the βγ-double bond is easily understood, but the complete stereospecificity of the hydrogenation is surprising; approach of an activated hydrogen molecule from the side unobstructed by the carboxyl group, giving the *cis*-isomer, is evidently far more probable.

The ultra-violet absorption spectra of the compounds discussed are:

Substance	(I)	(IV) *	(II)	(V) *	(III)	Methyl but-2-ynoate
$\lambda_{max.}$, Å	<2000	<2000	<2000	<2000	2055	2060
ε	(110) †	(630) †	(6400) †	(8300) †	6300	7200

* Purest specimen obtained. † At 2100 Å.

Experimental

In the work described below, infra-red absorption spectra were determined with a Perkin–Elmer Double-Beam Spectrometer, Model 21; ultra-violet spectra with a Unicam SP500 Spectrophotometer, in 95% ethanol; and melting-points with the Kofler block.

Buta-2 : 3-dienoic Acid (II).—But-3-ynoic acid (5·0 g.) was treated with potassium carbonate solution (18%; 200 c.c.) at 40° for 3 hr. After acidification and isolation with ether the *acid* (4·6 g.) had m. p. 61—63°, raised to 65—66° by crystallisation from light petroleum (Found: C, 57·25; H, 4·7%; equiv., 84·2. $C_4H_4O_2$ requires C, 57·15; H, 4·8%; equiv., 84·1).

But-2-ynoic Acid (III).—Buta-2 : 3-dienoic acid (4·0 g.) was treated with potassium carbonate solution (18%; 300 c.c.) at 90° for 8 hr. After acidification, extraction with ether, and recrystallisation from light petroleum (b. p. 60—80°) the product (2·4 g.) had m. p. 75—76°, undepressed on admixture with an authentic specimen of tetrolic acid.

Ethyl But-3-ynoate (IV).—A solution of but-3-ynoic acid (32 g.) in ethanol (270 c.c.) and sulphuric acid (10 c.c.) was set aside at 20° for 10 days. Isolation of the neutral fraction with especial care to minimise contact with alkaline solutions gave the *ester* (33 g.), b. p. 104—105°/190 mm., n_D^{19} 1·4291 (Found: C, 63·8; H, 7·2. $C_6H_8O_2$ requires C, 64·3; H, 7·2%).

Ethyl Buta-2 : 3-dienoate (V).—(*a*) A solution of but-3-ynoic acid (32 g.) in ethanol (200 c.c.) and sulphuric acid (12 c.c.) was set aside at 20° for 7 days. An excess of a saturated solution of potassium carbonate was added and the solution was filtered. After removal of most of the ethanol by distillation and addition of water (800 c.c.) the neutral fraction was isolated with ether and distilled, giving the *ester* (19 g., 44%), b. p. 44°/130 mm., n_D^{19} 1·4585 (Found: C, 64·65; H, 7·3. $C_6H_8O_2$ requires C, 64·25; H, 7·2%). The residue from the distillation was ethyl β-ethoxycrotonate (*ca.* 8 g.). Infra-red absorption data revealed the presence of a trace of the βγ-acetylenic ester (IV) in the allenic ester.

(*b*) Ethyl but-3-ynoate (1·1 g.) was shaken with 10% potassium carbonate solution (10 c.c.) for 10 min., and the suspension was set aside for 16 hr. Isolation with ether gave the allenic ester (0·9 g.), $n_D^{20\cdot5}$ 1·4555 unchanged on repetition of this alkaline treatment. A somewhat greater quantity of the acetylenic ester than in the specimen described above (~10%) appeared to be present.

The ester reacted only slowly with bromine in carbon tetrachloride, iodine in ethanolic potassium iodide, or ozone at 20°; it did not polymerise when warmed to 100° with benzoyl peroxide or on treatment with boron trifluoride.

Ethyl β-Ethoxycrotonate (VI).—Ethyl but-3-ynoate (1·1 g.) was added dropwise to a solution of sodium ethoxide (from sodium, 0·23 g.) in ethanol. When the exothermal reaction ceased, the neutral fraction (1·45 g.) was isolated with ether; it solidified completely and had m. p. 30°, undepressed on admixture with an authentic specimen of ethyl β-ethoxycrotonate, m. p. 30°.

Ethyl β-Piperidinocrotonate.—Piperidine (0·85 g.), ethyl buta-2 : 3-dienoate (1·12 g.), and ether (10 c.c.) were warmed under reflux for 3 hr. Distillation then gave the ester (1·05 g.), b. p. 110° (bath temp.)/0·03 mm., n_D^{16} 1·5392 (Found: C, 66·9; H, 9·4; N, 7·1. Calc. for $C_{11}H_{19}O_2N$: C, 67·0; H, 9·7; N, 7·1%). (Feist, *Annalen*, 1906, **345**, 100, gives b. p. 169°/15 mm.) Light absorption: max., 2870 Å, ε = 24,700.

Ethyl β-Anilinocrotonate.—Aniline (0·93 g.) and ethyl buta-2 : 3-dienoate (1·12 g.) similarly gave the anilino-ester (1·15 g.), b. p. 106°/0·5 mm., n_D^{16} 1·5820 (Found: N, 7·0. Calc. for $C_{12}H_{15}O_2N$: N, 6·8%). (Coffey, Thompson, and Wilson, *J.*, 1936, 859, give b. p. 137—139°/6 mm.) Light absorption: max., 3010 Å, ε = 20,400.

Ethyl β-p-Ethoxyanilinocrotonate.—This was similarly prepared from *p*-phenetidine (0·68 g.) and the ester (V) (0·56 g.). After chromatographic purification and crystallisation from *iso*propyl

ether, the ester (0·95 g.) had m. p. and mixed m. p. 53—54°. Light absorption: max., 2960 Å, $\varepsilon = 22{,}800$.

A somewhat lower yield was obtained when the amine and ester were mixed at room temperature without a diluent; the temperature rose at once to 90°, necessitating external cooling.

Polymerisation of Buta-2 : 3-dienoic Acid.—A solution of the allenic acid (II) (500 mg.) in xylene (5 c.c.) was heated under reflux for 1 hr. Evaporation of the solid and sublimation at 0·1 mm. gave dehydracetic acid (60 mg.), m. p. and mixed m. p. 110° after recrystallisation from pentane. The infra-red spectrum was identical with that of an authentic specimen.

Hydrogenation of Buta-2 : 3-dienoic Acid.—A solution of the allenic acid (2·0 g.) in ethyl acetate (100 c.c.) was shaken in hydrogen with a palladium–calcium carbonate catalyst (1·5% Pd; 1 g.). After the compound had absorbed 1 mole (18 min.) of hydrogen the catalyst and solvent were removed; a portion of the residue (2·0 g.) was dissolved in carbon disulphide, and its infra-red spectrum was examined. Bands at 1940, 990, and 690 cm.$^{-1}$ were absent, which excludes the possibilities that buta-2 : 3-dienoic, vinylacetic, and *trans*-crotonic acid, respectively, were present in significant quantity. Bands at 820 cm.$^{-1}$ and 729 cm.$^{-1}$ were observed, the intensities approaching those of an authentic sample of *cis*-crotonic acid at these frequencies. Another portion (0·50 g.) was treated with bromine (0·93 g.) in carbon tetrachloride (5 c.c.); evaporation of the solvent and recrystallisation from pentane gave *threo*-αβ-dibromobutyric acid (1·0 g.), m. p. 58—59° (Michael and Schulthess, *J. prakt. Chem.*, 1892, **46**, 241, give m. p. 59°).

Vinylacetic Acid and But-3-en-1-ol.—Buta-2 : 3-dienoic acid (II) (5·0 g., 0·059 mol.) in ether (50 c.c.) was added dropwise to an ethereal solution of lithium aluminium hydride (435 c.c.; containing 0·049 mol.) at −20° during 1·5 hr. Addition of water and sulphuric acid, and separation into acidic and neutral portions, gave but-3-en-1-ol (0·85 g.), b. p. 112°/767 mm., n_D^{21} 1·4180. Because of confusion in the literature on this compound, an authentic specimen was prepared by incomplete semihydrogenation of but-3-yn-1-ol; the acetylenic alcohol (but not butan-1-ol) can readily be separated from but-3-en-1-ol by fractional distillation. This had b. p. 115°/752 mm. (a more reliable figure than that of the small-scale distillation), n_D^{21} 1·4198. Both specimens gave an *α-naphthylurethane*, m. p. 76—77°, undepressed on admixture (Found: C, 74·75; H, 6·2; N, 5·5. $C_{15}H_{15}O_2N$ requires C, 74·65; H, 6·25; N, 5·8%), and their infra-red spectra were identical.

Distillation of the acid fraction gave vinylacetic acid (1·18 g.), b. p. 85° (bath temp.)/16 mm., n_D^{23} 1·4218 (Linstead, Noble, and Boorman, *J.*, 1933, 560, give b. p. 72°/14 mm., n_D^{20} 1·4220). Bromination gave βγ-dibromobutyric acid, m. p. 49—50° (Fichter and Sonneborn, *Ber.*, 1902, **35**, 938, give m. p. 49—50°).

A similar reduction of ethyl buta-2 : 3-dienoate gave ethyl vinylacetate, b. p. 75°/130 mm., n_D^{21} 1·4110 (Bruylants, *Bull. Soc. chim. Belg.*, 1929, **38**, 163, gives b. p. 124°/755 mm., n_D^{20} 1·4105) (Found: C, 62·6; H, 9·3. Calc. for $C_6H_{10}O_2$: C, 63·15; H, 8·85%). A small quantity of but-3-en-1-ol was also present.

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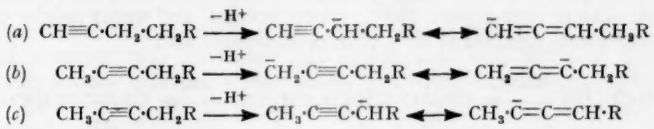
Researches on Acetylenic Compounds. Part XLVI. Prototropic Rearrangements of Acetylenic Acids.*

By E. R. H. Jones, G. H. Whitham, and M. C. Whiting.

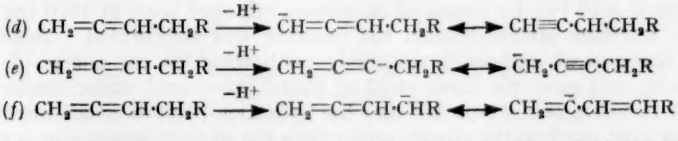
[Reprint Order No. 5304.]

Acetylenic acids may undergo prototropic rearrangements in alkaline solution to give isomeric compounds of the acetylenic, allenic, or conjugated dienoic acid types. The direction and relative rates of these changes, superficially in some cases surprising, are explained in terms of the known energy relationships between the different unsaturated groupings present in the products and in their carbanion intermediates. Hyperconjugation is shown to play a more important role than in the transformation of the related ethylenic compounds.

The isomerisation of acetylenic hydrocarbons under alkaline conditions, a much easier process than that of the corresponding ethylenes, was discovered by Favorskii (*J. Russ. Phys. Chem. Soc.*, 1887, **19**, 414; *J. prakt. Chem.*, 1888, **37**, 382). It has recently been greatly clarified by Jacobs, Akawie, and Cooper (*J. Amer. Chem. Soc.*, 1951, **73**, 1273), who demonstrated that pent-1-yne, pent-2-yne, and penta-1 : 2-diene are each converted by contact with alcoholic potassium hydroxide at 175° into a mixture of all three, containing at equilibrium about 1·3%, 95·2%, and 3·5%, respectively. Under these conditions penta-2 : 3-diene, and penta-1 : 3-diene, presumably the most stable isomer, are not formed at an appreciable rate. If it is assumed that interconversion proceeds *via* carbanion intermediates (see below), this implies that of the three formally very similar processes (*a*, *b*, and *c*; R = CH_3), both (*a*) and (*b*) are considerably faster than (*c*). That the carbanion in (*a*)



is more readily formed than that in (*c*) may be correlated with the evidence that an alkyl group partly neutralises the electron-attracting power of the acetylenic linkage in propiolic acid ($K_a = 14 \times 10^{-3}$; cf. tetrolic acid, $K_a = 2{\cdot}46 \times 10^{-3}$). The advantage of (*b*) over (*c*) is explained by the relative stability of the simple carbanions, methyl > primary > secondary > tertiary, as indicated by the reverse order of reactivity in elimination reactions on saturated ethers (see, *inter al.*, Gilman, Moore, and Baine, *J. Amer. Chem. Soc.*, 1941, **63**, 2479) and by the tendency of tertiary carbanions to add to ethylene (Bartlett, Friedman, and Stiles, *J. Amer. Chem. Soc.*, 1953, **75**, 1771). Under more drastic conditions the reaction (*c*) and obvious subsequent stages do take place (see, *inter al.*, Bourgel, *Ann. Chim.*, 1925, **3**, 325).



The behaviour of penta-1 : 2-diene implies that processes (*d*) and (*e*) are faster than (*f*). When allenes and acetylenes are treated with acidic oxides, *e.g.*, "floridin," somewhat similar transformations ensue, but conjugated dienes are then formed in quantity, indicating that the energy relationships among the various unsaturated carbonium ions are quite different.

* Part XLV, preceding paper.

The isomerisations of acetylenic hydrocarbons are the necessary basis for understanding the observations described in the present and several subsequent papers in this Series; hence the need for the generalisations above. These reactions are also of some interest from the synthetical standpoint, especially since the products can usually be reduced specifically to the corresponding *cis*- or *trans*-olefins. Potentially more important in this second respect are similar transformations in acetylenic compounds bearing functional groups, but the only examples previously recorded are the conversion of the terminally acetylenic acids, undec-10-ynoic and tricos-22-ynoic acids, into their isomers containing $CH_3{\cdot}C{\equiv}C{\cdot}$ groups (Krafft, *Ber.*, 1896, **29**, 2232; Stenhagen, *Arkiv Kemi*, 1949, **1**, 99). The preceding paper describes an investigation of the prototropic rearrangements of the acids, $C_3H_4{\cdot}CO_2H$, and the present contribution deals with other doubly-unsaturated acids of moderate chain-length and without lateral substitution. Subsequent papers in this Series will outline the extension of these studies to a variety of acetylenic acids and other derivatives. The preparation of the ω-acetylenic acids used as starting-materials has been described by Eglinton and Whiting (*J.*, 1953, 3052).

Pent-4-ynoic acid (I) was treated with potassium hydroxide under varied conditions in preliminary experiments. Although such mild reagents as sufficed to isomerise but-3-ynoic acid had no effect, boiling 9N-potassium hydoxide converted it into penta-2 : 4-dienoic acid (III) in a maximal yield of 60% (spectroscopic, after 1 hour; 40% isolated). Presumably this must be formed by a second prototropic transformation of penta-3 : 4-dienoic acid (II):

$$\underset{\text{(I)}}{CH{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H} \xrightarrow{HO^-} \underset{\text{(II)}}{CH_2{=}C{=}CH{\cdot}CH_2{\cdot}CO_2H} \xrightarrow{HO^-} \underset{\text{(III)}}{CH_2{=}CH{\cdot}CH{=}CH{\cdot}CO_2H}$$

but interruption of the reaction and infra-red examination of the product did not reveal the presence of (II). Mr. P. Nayler has prepared this allenic acid by oxidation of penta-3 : 4-dien-1-ol (Bates, Jones, and Whiting, *J.*, 1954, 1854), and showed that it isomerises to penta-2 : 4-dienoic acid in higher yield (80%, spectroscopic), and under milder conditions (10% potassium carbonate solution at 60°), than pent-4-ynoic acid.

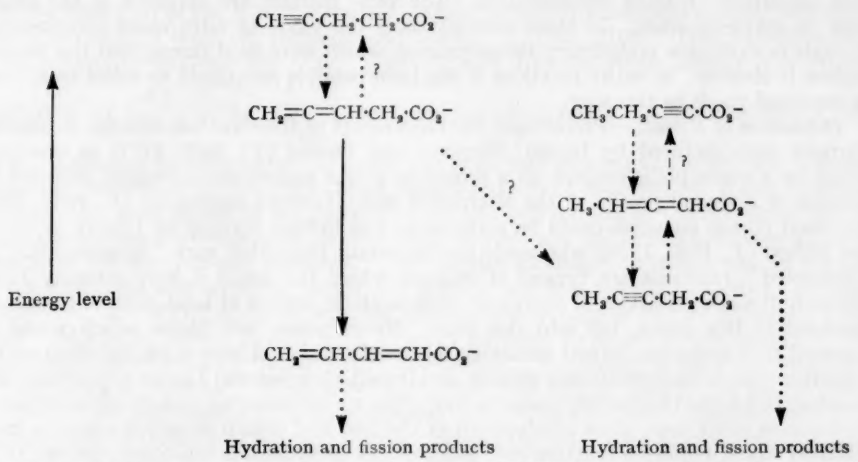
$$CH{\equiv}C{\cdot}CH{=}CH{\cdot}CH_2{\cdot}OH \xrightarrow{LiAlH_4} CH_2{=}C{=}CH{\cdot}CH_2{\cdot}CH_2{\cdot}OH \xrightarrow{CrO_3} \underset{\text{(II)}}{CH_2{=}C{=}CH{\cdot}CH_2{\cdot}CO_2H}$$

Attention was then directed to pent-3-ynoic acid (IV), the preparation of which is discussed below. This acid was apparently converted into either penta-2 : 3-dienoic or pent-2-ynoic acid under fairly drastic conditions, since the hydration product, ethyl methyl ketone, was formed in boiling aqueous 9N-potassium hydroxide, while ethylene glycol and potassium hydroxide gave the dioxalan derived from propionylacetic acid. Nevertheless these isomeric acids were not formed to any appreciable extent and could not be isolated. On the contrary, pent-2-ynoic acid was isomerised in 9N-potassium hydroxide at 60° to the Δ^3-isomer, which was isolated without difficulty since it is relatively high melting, in 64% yield, and thus clearly predominates in the equilibrium mixture. Here again an allenic acid must be assumed as an intermediate, but this time it proved possible to identify the penta-2 : 3-dienoic acid (V), by means of its intense infra-red band at 1970 $cm.^{-1}$, in the syrupy acidic fractions obtained when the reaction was interrupted. This acid was prepared by the present authors (forthcoming publication) in the course of quite independent work, and gave the same yield of pent-3-ynoic acid under similar alkaline conditions; it therefore seems probable that the hydration reaction which interferes with the prototropic shift involves the allenic, rather than the αβ-acetylenic anion, a conclusion in harmony with that drawn about the relative reactivity towards nucleophilic reagents of tetrolic and butadienoic esters in the preceding paper. Because of the formation of ethyl methyl ketone even at 60°, the proportion of pent-3-ynoic acid present in (hypothetical) equilibrium with its two isomers must presumably be more than the 60% actually isolated.

The Figure illustrates the transformations of the doubly-unsaturated C_5 straight-chain acids, all of which (except *cis*-penta-2 : 4-dienoic) have now been prepared. The speed of

each reaction, as judged by the severity of the conditions required for it, is very roughly indicated by the type of line used; and the ordinate may be taken as a qualitative representation of free energy in strongly alkaline solutions, where only the derived anions need be considered. There is no means, however, of comparing directly the acids on the left with the group on the right.

FIGURE.



The symbols ⟶, ⇢, -·-·►, and ····► indicate reaction rates diminishing approximately in that order; transformations queried have not been observed but are known to be possible from the behaviour of analogous systems.

No attempt has been made to investigate every acid in the C_6 and C_7 series. Hex-5-ynoic acid, however, was converted into hex-4-ynoic acid (82%) in boiling (138°) 15N-potassium hydroxide solution, under which conditions its homologue, hept-6-ynoic acid,

TABLE.

Reagent	Temp.	Reaction	Yield, %	Time, hr.
*A**	40°	$CH{\equiv}C{\cdot}CH_2{\cdot}CO_2^- \longrightarrow CH_2{=}C{=}CH{\cdot}CO_2^-$	92	3
A	60	$CH_2{=}C{=}CH{\cdot}CH_2{\cdot}CO_2^- \longrightarrow CH_2{=}CH{\cdot}CH{=}CH{\cdot}CO_2^-$	80	2
*A**	90	$CH_2{=}C{=}CH{\cdot}CO_2^- \rightleftharpoons CH_3{\cdot}C{\equiv}C{\cdot}CO_2^-$	60 (⟶)	8
B	60	$CH_3{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CO_2^-$ or $CH_3{\cdot}CH{=}C{=}CH{\cdot}CO_2^- \longrightarrow CH_3{\cdot}C{\equiv}C{\cdot}CH_2CO_2^-$	61	1
B	118	$(CH_3{\cdot}C{\equiv}C{\cdot}CO_2^- \rightleftharpoons CH_2{=}C{=}CH{\cdot}CO_2^-) \longrightarrow$ hydration products		~2
B	118	$(CH_3{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CO_2^- \longleftarrow CH_3{\cdot}CH{=}C{=}CH{\cdot}CO_2^-) \longrightarrow$ hydration products		
B	118	$CH{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2^- \xrightarrow{2\text{ stages}} CH_2{=}CH{\cdot}CH{=}CH{\cdot}CO_2^-$	60	6
C	138	$CH{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2^- \xrightarrow{2\text{ stages}} CH_3{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2^-$	82	1
D	160	$CH_3{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2^- \xrightarrow{2\text{ stages}} CH_3{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CO_2^-$	93	1
D	160	$CH{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2^- \xrightarrow{2\text{ stages}} CH_3{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2^-$	33	1

Reagents: *A*, 10% K_2CO_3; *A**, 18% K_2CO_3; *B*, 9N-KOH; *C*, 15N-KOH; *D*, 9N-KOH in ethylene glycol.

was quite stable. (Hex-5-ynoic acid was similarly unaffected by 9N-potassium hydroxide at 118°, which rapidly isomerised pent-4-ynoic acid.) When treated with 9N-potassium hydroxide in ethylene glycol at 160°, however, hept-6-ynoic acid was isomerised to hept-5-ynoic acid, though (perhaps because of its low melting-point) only a 33% yield could be

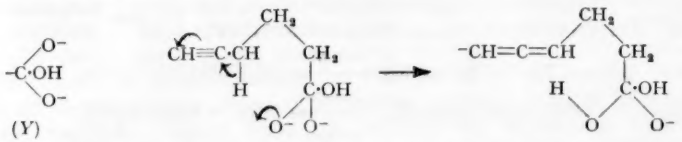
isolated. These conditions also sufficed to convert hex-4-ynoic acid almost quantitatively into sorbic acid. Hept-5-ynoic acid, on the other hand, resisted this reagent for considerable periods, and apparently underwent fission rather than isomerisation to a conjugated dienoic acid.

The Table summarises the isomerisations of the doubly-unsaturated acids investigated, and illustrates the extreme sensitivity of reaction rates to temperatures and—probably more important—reagent concentration. The same features are apparent in the earlier work on ethylenic acids. In these circumstances the value of ultra-violet spectroscopic methods in extensive preliminary investigations, which were used throughout the present studies, is obvious; in many reactions it has been possible accurately to select conditions for maximal yields in this way.

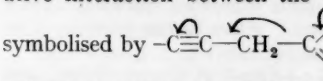
Discussion of Results.—Prototropic rearrangements of three-carbon systems in alkaline solutions were pictured by Ingold, Shoppee, and Thorpe (*J.*, 1926, 1477) as involving attack by a nucleophilic reagent on a proton to give a mesomeric carbanion, followed by addition of a second proton at the alternative site. Lowry's suggestion (*J.*, 1925, 2883) that dual proton transfers could be sychronous was further verified by Ingold, de Salas, and Wilson (*J.*, 1936, 1328), who made the important point that such " termolecular " or " concerted " reactions are typical of systems where the anion is very strongly basic. Probably the isomerisations of acetylenic hydrocarbons, and of at least most of the anions discussed in this paper, fall into this class. Nevertheless, any factor which would be expected to stabilise the formal carbanion intermediate should have a similar effect on the transition state in the termolecular process, and Ingold, Shoppee, and Thorpe's hypothesis will therefore be adopted to simplify presentation. The species suffering prototropy is obviously the anion in every case, since involvement of the free acid (which should of course be more reactive) would require a reaction-rate independent of hydroxide-ion concentration, HO^-, or some other species proportional to HO^-, being assumed to be the nucleophilic agent.

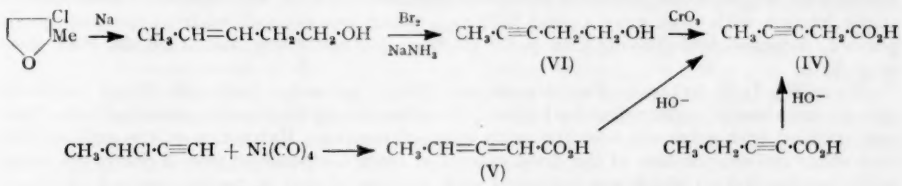
Much of the behaviour of the acetylenic acids (*e.g.*, the difference in rate of reaction between pent-4-ynoic and hex-4-ynoic acids) parallels that of the acetylenic hydrocarbons as generalised and interpreted above. The presence of a CO_2^- grouping controls the prototropy of the anion of penta-3 : 4-dienoic acid by facilitating the removal of a proton from $C_{(2)}$ [in contrast to (*d*, *e*) > (*f*) above, where R = Me], which results in the formation of penta-2 : 4-dienoic, rather than pent-3-ynoic, acid anion.

The rates of isomerisation of pent-4-ynoic and hex-5-ynoic acids, relative to hept-6-ynoic and higher ω-acetylenic acids and ω-acetylenic hydrocarbons, are also of interest. The proximity of $-CO_2^-$ is evidently important, and since inductive influence is implausible, especially in the case of hex-5-ynoic acid, participation of this grouping in the prototropic process is probable. The $-CO_2^-$ group, a weak base, could not of course be involved as such, since this would imply that no additional alkaline reagent was required; but reversible addition of HO^- to the carbonyl group would give the grouping (*Y*), which might well effect an internal attack:



Finally, we find that pent-3-ynoic acid is appreciably more stable than either the Δ^2-acetylenic or the $\Delta^{2:3}$-allenic C_5 acids in alkaline solution. This system is difficult to investigate because of the lack of convenient analytical methods, and Mr. J. M. Thompson's observations (forthcoming publication) on the isomerisations of the corresponding di- and tri-acetylenic acids, $CH_3{\cdot}CH_2{\cdot}[C{\equiv}C]_n{\cdot}CO_2H$, are more clear-cut. Even in the present instance, however, it seems clear that if true equilibrium could be attained, at least twice as much of the Δ^3-acid anion as of the other two isomers combined would be present. Even the minimal value for the ratio (pent-3-ynoate/pent-2-ynoate), say 3, contrasts sharply with the analogous ratio, 0·61, found by Ives and Kerlogue (*J.*, 1940, 1362) for the pentenoic

acid system; and the true value is probably much higher. One simple explanation involves the geometrical requirements of interaction between acetylenic and ethylenic bonds, on the one hand, and $-CO_2^-$ and $-CH_3$ or $-CH_2-$ groupings, on the other. In conjugative interaction with $-CO_2^-$, which is planar, only one of the two π-electron pairs of a triple bond can be involved, so that an acetylenic linkage will have no advantage over an ethylenic linkage. In hyperconjugative interaction with the σ electrons of the C–H bonds in a methyl group, however, the cylindrically symmetrical electron cloud of the triple bond will be more effective than that of the planar ethylenic linkage, which probably can interact efficiently with only one C–H bond (cf. Baddeley and Gordon, *J.*, 1952, 2190). Direct hyperconjugative interaction between the $-CO_2^-$ grouping and a $\beta\gamma$-acetylenic linkage (the process symbolised by  ; applying less effectively in $\beta\gamma$-ethylenic carboxylate anions) is another possible factor. Finally, one must take account of the intrinsic electron-attracting tendencies of the triple bond, which have been ascribed by Walsh (*Discuss. Faraday Soc.*, 1947, **2**, 18) to the polarity of the *sp*-bond formed by the acetylenic carbon atom, the increased *s*-component (as compared with sp^2 and sp^3 bonds) involving a tighter binding of the electron-pair involved. This implies an inductive interaction of the unsaturated linkage with adjacent groups, the effect of which is difficult to predict; it might be expected that $-CO_2^-$, electron-repelling in saturated systems as a result of large $+I$ and small $-M$ effects, should be still more so when adjacent to an acetylenic linkage. This should stabilise $-C{\equiv}C-CO_2^-$ relative to $-CH{=}CH{\cdot}CO_2^-$, *i.e.*, should act in a contrary sense to that which is observed. Work now in progress may help to disentangle the problems involved in the explanation of these equilibria; meanwhile the results obtained exemplify the fundamental differences between the chemistry of the ethylenic and acetylenic linkages.



Appendix.—The preparative work involved in this study conflicts with the literature in two instances, involving substances previously described as pent-3-ynoic and hex-3-ynoic acids. The first was reported by Schjånberg (*Ber.*, 1938, **71**, 569) as one product (5% yield) of the action of potassium hydroxide on 3 : 4-dibromopentanoic acid. Its melting-point was given as 52·5°, near to its acetylenic isomers (57° and 50·5°), its structure was not proved by degradative methods and the method of synthesis clearly does not provide sufficient evidence of constitution. In seeking a convenient method of preparation before the discovery of the prototropic rearrangements discussed above we utilised the alcohol (VI), reported by Crombie and Harper (*J.*, 1950, 877). On oxidation with chromic acid in acetone this gave an acid, $C_5H_6O_3$, m. p. 101—104°, different from pent-2-ynoic and pent-4-ynoic acids, yet optically transparent above 2000 Å ($\varepsilon \not> 400$). Its methyl ester showed infra-red absorption bands [at 2240 cm.$^{-1}$ (weak) and 1741 cm.$^{-1}$ (strong); none between 1600 and 1720 cm.$^{-1}$] which provided final confirmation that it was indeed pent-3-ynoic acid, (IV). The nature of Schjånberg's acid remains doubtful; its ethyl ester differed in refractive index by 0·005 from that of (IV), and the possibility that it was a polymorphic form of (IV) seems remote.

Marayuma and Suzuki (see *Chem. Abs.*, 1932, **26**, 1879; 1935, **29**, 1062) claimed that sorbic acid (m. p. 134°) is converted by potassium hydroxide in ethanol at 180° into " hex-3-ynoic acid," m. p. 128°. The structure of their product, *a priori* a most surprising one, was supported only by oxidation to propionic acid. We prepared hex-3-ynoic acid by oxidation of the corresponding primary alcohol (Eglinton, Jones, and Whiting, *J.*, 1952, 2873) with chromic acid, and found that its melting-point was 60—61°. Its structure was

proved by hydrogenation to hexanoic acid, by permanganate oxidation to malonic acid, and by its optical transparency ($\varepsilon \gg 100$ above 2020 Å). We then repeated the Japanese workers' experiment, and isolated, as expected, merely unchanged sorbic acid (60% recovery), m. p. and mixed m. p. 134° when pure; thus their product was probably impure starting material.

Experimental

Ultra-violet spectra were determined in 95% ethanol by using a Unicam SP500 Spectrophotometer, and infra-red spectra in carbon tetrachloride (unless otherwise specified) with a Perkin Elmer Model 21 Spectrophotometer. "Light petroleum" refers to the fraction, b. p. 40—60°. Melting points were determined on the Kofler block.

Penta-3 : 4-dienoic Acid (II) (*with* P. Nayler).—Penta-3 : 4-dien-1-ol (Bates, Jones, and Whiting, *J.*, 1954, 1854; 5 g.) in acetone (37 c.c.) was treated with chromic acid solution (37 c.c.; as below) during 40 min. at 10°. After a further 15 hr. at 20° the mixture was diluted with water, and the acidic fraction was isolated with ether. Distillation gave *penta-3 : 4-dienoic acid* (1·35 g.), b. p. 127°/13 mm. (slight decomp.), n_D^{18} 1·4740 (Found: C, 60·85; H, 6·9%; equiv., 98. $C_5H_6O_2$ requires C, 61·2; H, 6·1%; equiv., 98). Light absorption: no maximum above 2000 Å; $\varepsilon = 960$ at 2200 Å. The liquid absorbed intensely at 1967 cm.$^{-1}$ in the infra-red, but showed no strong bands in the $>C{=}C<$ stretching region at 1600—1650 cm.$^{-1}$. The *p-bromophenacyl* ester formed plates, m. p. 65°, from methanol (Found: C, 52·75; H, 3·85. $C_{23}H_{11}O_3Br$ requires C, 52·9; H, 3·73%). It absorbed intensely at 1970 cm.$^{-1}$.

Distillation of the neutral fraction from the oxidation mixture gave *penta-3 : 4-dienyl penta-3 : 4-dienoate* (1·3 g.), b. p. 115°/18 mm., n_D^{24} 1·4895 (Found: C, 72·9; H, 7·4. $C_{10}H_{12}O_2$ requires C, 73·2; H, 7·3%).

Penta-2 : 4-dienoic Acid.—(*a*; *with* P. Nayler.) Penta-3 : 4-dienoic acid (230 mg.) was heated with 10% aqueous potassium hydroxide solution (20 c.c.) at 60° for 2 hr. Isolation of the acidic fraction with ether gave a solid (220 mg.) which was crystallised from pentane, giving penta-2 : 4-dienoic acid (180 mg.), m. p. 71° (Kohler, *J. Amer. Chem. Soc.*, 1926, **48**, 1041, gives m. p. 72°).

(*b*; *with* J. L. H. Allan.) Pent-4-ynoic acid (2·0 g.), potassium hydroxide (25 g.), and water (50 c.c.) were heated under reflux for 1·5 hr. The solution was then cooled, extracted with ether, and acidified with sulphuric acid (3N) with external cooling. Extraction of the acid solution with ether and evaporation of the dried extract at room temperature gave a partly polymeric acidic residue (1·3 g.) which was extracted with pentane, giving on cooling penta-2 : 4-dienoic acid (0·7 g.), m. p. 51—70°, the infra-red spectrum of which agreed almost exactly with that of the pure acid (0·4 g.), m. p. 71—73°, obtained after sublimation and four recrystallisations from pentane at 20°. Light absorption; maximum 2420 Å, $\varepsilon = 24{,}800$.

This experiment was based on spectroscopically-controlled runs; preparatively, the volume of solution used could be greatly reduced. When a 5 : 2 water–alcohol mixture was used as solvent, with a reaction-period of 6 hr. at 100°, the spectroscopic yield of pentadienoic acid was 60%.

Pent-3-ynoic Acid (IV).—(*a*; *preparative method, with* G. H. Mansfield.) Pent-2-ynoic acid (5·0 g.; Zoss and Hennion, *J. Amer. Chem. Soc.*, 1941, **63**, 1151), potassium hydroxide (5 g.), and water (to 50 c.c.) were heated to 60° for 1 hr. Cautious acidification of the cooled solution, isolation of the acidic fraction and crystallisation from benzene–light petroleum (b. p. 60—80°) gave the *acid* (3·2 g.), m. p. 103—104°. When the oil (1·0 g.) remaining in the mother-liquors was recycled a further 0·3 g. of pent-3-ynoic acid, m. p. 102—103°, was obtained (Found: C, 60·9; H, 6·4. $C_5H_6O_2$ requires C, 61·2; H, 6·15%).

(*b*) Penta-2 : 3-dienoic acid (200 mg.; Jones, Whitham, and Whiting, forthcoming publication) was treated with alkali as above, yielding pent-3-ynoic acid (106 mg.), m. p. and mixed m. p. 103—104°.

(*c*) 6N-Chromic acid in 12N-sulphuric acid (300 c.c.) was added with stirring and cooling to a solution of pent-3-yn-1-ol (29·4 g.; Crombie and Harper, *J.*, 1950, 877) in acetone (300 c.c.), the temperature being kept at 25°. Isolation of the acid fraction after 4 hr. gave the acid, which crystallised from light petroleum (b. p. 60—80°) as flat needles (16 g., 50%), m. p. 101—104° (Found: C, 60·9; H, 6·4%).

Pent-3-yn-1-ol was also obtained in small yield from prop-1-ynylmagnesium bromide and ethylene oxide (Iositch, *Bull. Soc. chim.*, 1909, **6**, 98). Unexpectedly the ring-fission of 3-chloro-

2-methyltetrahydrofuran with sodamide was also unsatisfactory, the main products being methyldihydrofurans (cf. Eglinton, Jones, and Whiting, *J.*, 1952, 2873).

2-Ethyl-1 : 3-dioxalan-2-ylacetic Acid.—Pent-3-ynoic acid (2 g.), ethylene glycol (20 c.c.), and potassium hydroxide (5 g.) were heated under reflux during 1 hr. After dilution and acidification of the solution, the acid fraction was isolated with ether, giving the *dioxalan* (1·4 g., 43%), b. p. 130° (bath temp.)/0·05 mm., n_D^{18} 1·4530 (Found: C, 52·7; H, 7·5. $C_7H_{12}O_4$ requires C, 52·5; H, 7·55%).

The dioxalan (0·43 g.) was heated with 20% sulphuric acid (30 c.c.), and the mixture distilled. Addition of 2 : 4-dinitrophenylhydrazine sulphate solution to the aqueous distillate gave a precipitate which crystallised from ethanol as brick-red needles (0·42 g., 62%), m. p. 115—117° undepressed on admixture with an authentic specimen of ethyl methyl ketone 2 : 4-dinitrophenylhydrazone.

Hex-3-ynoic Acid.—6N-Chromic acid (22 c.c.) was added to a cooled, stirred solution of hex-3-yn-1-ol (2·9 g.; Eglinton, Jones, and Whiting, *loc. cit.*) in acetone (22 c.c.) during 30 min., the temperature being maintained at 20°. The solid acid fraction, on crystallisation from light petroleum (b. p. 40—60°), gave the *acid* (0·77 g., 24%) as fine needles, m. p. 57—59°, raised to 61—63° on recrystallisation (Found: C, 64·5; H, 7·5. $C_6H_8O_2$ requires C, 64·25; H, 7·2%). The structure was proved by oxidation with potassium permanganate to malonic acid, m. p. 134·5—135°, in 18% yield.

Hex-4-ynoic Acid.—Hex-5-ynoic acid (1·0 g.) was heated under reflux with 15N-potassium hydroxide during 1 hr. After acidification, the acid fraction was isolated with ether and crystallised from light petroleum giving the *acid* (0·82 g., 82%), as rhombohedral needles, m. p. 100—101° (Found: C, 64·5; H, 7·5. $C_6H_8O_2$ requires C, 64·25; H, 7·2%). Its structure was proved by oxidation with potassium permanganate to succinic acid (68% yield), m. p. and mixed m. p. 186—187°. The *methyl* ester had b. p. 61·5°/10 mm., n_D^{16} 1·4440 (Found: C, 66·5; H, 7·95. $C_7H_{10}O_2$ requires C, 66·65; H, 8·0%). It gave no precipitate with ammoniacal silver nitrate.

Sorbic Acid.—Hex-4-ynoic acid (1·00 g.) and 9N-potassium hydroxide in ethylene glycol (10 c.c.) were heated to 160° for 1 hr. Dilution, acidification, and isolation with ether gave the acid (0·93 g.) as prismatic needles, m. p. and mixed m. p. 134—135°.

Hept-5-ynoic Acid.—Hept-6-ynoic acid (1·00 g.) and 9N-potassium hydroxide in ethylene glycol (10 c.c.) were heated to 160° for 1 hr. Distillation of the acid fraction gave an oil, b. p. 90° (bath temp.)/0·05 mm., n_D^{20} 1·4649, which solidified to a mass of needles, m. p. *ca.* 27°. After recrystallisation from light petroleum (b. p. 40—60°) the *acid* (0·33 g., 33%) was obtained as translucent plates, m. p. 36—38° (Found: C, 66·25%; H, 8·0%). Oxidation with permanganate gave glutaric acid, m. p. 95—96°, in 33% yield.

The authors are indebted to the Department of Scientific and Industrial Research for a grant to one of them (G. H. W.). They thank Miss W. Peadon and Miss J. Shallcross for spectroscopic measurements, and Messrs. E. S. Morton and H. Swift for microanalyses.

THE UNIVERSITY, MANCHESTER. [*Received, April 13th*, 1954.]

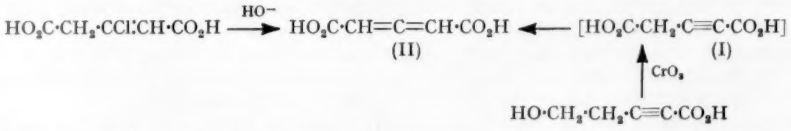
Researches on Acetylenic Compounds. Part XLVII. The Prototropic Rearrangements of Some Acetylenic Dicarboxylic Acids.*

By E. R. H. Jones, G. H. Mansfield, and M. C. Whiting.

[Reprint Order No. 5305.]

Prototropic rearrangements of some acetylenic dicarboxylic acids, yielding allenic or conjugated dienic isomers, are described. "Glutinic acid" is shown to have an allenic (II) rather than an acetylenic (I) structure.

The simplest acetylenic dicarboxylic acid capable of prototropy is "glutinic acid" (I), first described by Burton and Pechmann (*Ber.*, 1887, **20**, 148) as the product of the action of potassium hydroxide on β-chloroglutaconic acid. This method was much improved by van der Zanden (*Rec. Trav. chim.*, 1935, **54**, 289). The original structure has not, so far as is known, been questioned; nevertheless repetition of van der Zanden's work gave an acid which possessed structure (II) rather than (I), although its properties agreed well with the



literature description. Its ultra-violet absorption spectrum showed intense rising absorption at low wave-lengths, reaching $\varepsilon = 27{,}200$ at 2000 Å. This is consistent with (II), for which one would predict a spectrum similar to that of acrylic acid ($\lambda_{max.}$ below 2000 Å, where $\varepsilon = 7500$) but with molar extinction coefficients rather more than twice as great (Celmer and Solomons, *J. Amer. Chem. Soc.*, 1953, **75**, 1375, and unpublished work from these laboratories). It is quite inconsistent with (I), for which strong resemblance to tetrolic acid ($\lambda_{max.}$ 2055 Å, $\varepsilon = 6300$) would be expected. Infra-red data confirmed this conclusion; the crystalline acid in Nujol suspension showed no absorption in the 2250-cm.$^{-1}$ region, where all αβ-acetylenic acids absorb strongly, but did absorb at 1970 cm.$^{-1}$, just as does buta-2 : 3-dienoic acid. The methyl ester, prepared with diazomethane, showed maxima at 1970 cm.$^{-1}$ (allene) and 1720 cm.$^{-1}$, the latter band indicating the presence of only one type of carbonyl group, and consistent in its position with an αβ-ethylenic ester system; it was almost transparent near 2200 cm.$^{-1}$.

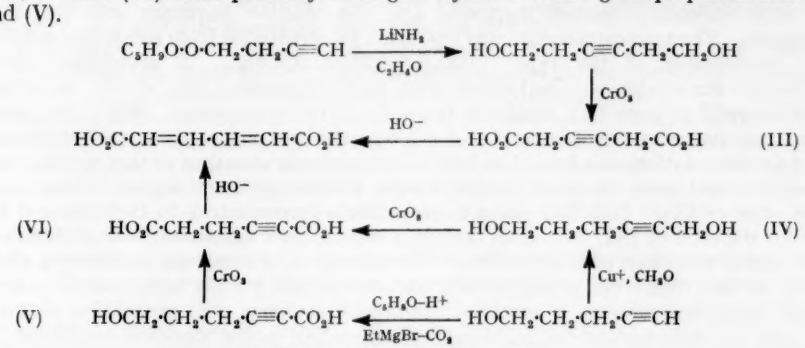
Consideration of the method of synthesis from chloroglutaconic acid suggested that the formation of (II) rather than (I) was to be expected. Kinetically, attack of hydroxyl ion on the doubly-activated protons of the methylene group should certainly predominate; thermodynamically, the equilibrium between (II) and (I) would probably favour the allenic isomer, though here the analogies available are less decisive (see preceding papers). An independent synthesis of (I) was therefore attempted; 5-hydroxypent-2-ynoic acid (Haynes and Jones, *J.*, 1946, 954) was oxidised with chromic acid in acetone, the use of even bicarbonate solution being avoided in the isolation of the product in the hope of preventing isomerisation. The product, obtained in 23% yield, again proved to be (II); thus equilibration of (I) and (II) must take place even in neutral or acidic solutions. Such exceptional mobility is, of course, understandable by analogy with the behaviour of glutaconic acid and its derivatives.

The two acids homologous to (I) were next examined.

One isomer (III) was readily obtained by oxidising the corresponding diprimary glycol (Raphael and Roxburgh, *J.*, 1952, 3875). The other (VI) was formed in the same way from the isomeric glycol (IV) (Paul and Tchelitcheff, *Bull. Soc. chim.*, 1953, 418) in much lower yield, and the alternative route *via* the hydroxy-acid (V) was therefore investigated, with equally mediocre results. In both cases the crude acid (VI) was contaminated with succinic acid, which was on one occasion isolated pure. Eglinton, Jones, and Whiting (*J.*, 1952, 2873) have discussed the abnormally rapid hydration of pent-4-yn-1-ol in acidic solution in

* Part XLVI, preceding paper.

terms of intramolecular nucleophilic attack by the hydroxyl group concerted with addition of a proton at $C_{(5)}$; presumably the hydroxy-acid (V), probably the first product from (IV), could undergo a similarly accelerated hydration reaction, giving a product convertible by further oxidation or hydrolysis into succinic acid. Mr. B. L. Shaw has observed (personal communication) that pent-4-ynoic acid similarly undergoes rapid hydration to lævulic acid, so that (VI) itself probably undergoes hydration during its preparation from (IV) and (V).

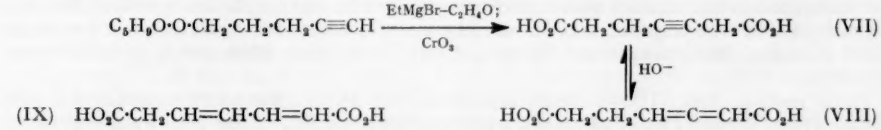


(C_5H_9O = 2-tetrahydropyranyl-)

The acid (III) rearranged to *trans-trans*-muconic acid in 9% potassium hydroxide solution at 40°; the yield was 44% (spectroscopic) and almost this quantity was isolated. Its isomer (VI) rearranged with greater difficulty (at 103° with the same reagent) and gave only a 23% yield (spectroscopic; 8% isolated). Presumably the hexa-2 : 3-dienedioic acid anion was the intermediate in both cases; the lower yield of muconic acid from (VI) might be due to either (*a*) a larger temperature coefficient for the rate of the competing hydration reaction than for the prototropic shift, or (*b*) some direct hydration of the anion of (VI) preceding its rearrangement to the allenic anion.

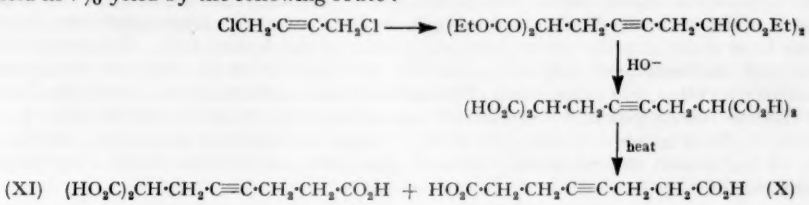
An ester, believed to be that of but-1-yne-1 : 3 : 4-tricarboxylic acid, and so related to (VI), gave muconic acid on vigorous alkaline hydrolysis (E. H. Ingold, *J.*, 1925, **127**, 1199). 1 : 4-Dichlorobut-2-yne and cuprous cyanide gave a dinitrile which underwent alkaline hydrolysis with rearrangement to muconic acid (Dr. J. Elvidge, personal communication).

The next acid examined, hept-3-ynedioic acid (VII), was prepared by the obvious route :



It was subjected to alkaline conditions of increasing severity, but no light absorption of appreciable intensity above 2200 Å could be discerned. Isolation of the product of the action of 9% potassium hydroxide solution at 90° and examination of its infra-red absorption spectrum indicated the presence of the allenic acid (VIII); evidently the equilibrium between (VII) and (VIII) is fairly readily established, but (VIII) is further converted into fission products rather than into (IX) or sorbic acid.

Finally the acid (X) was prepared. Johnson (*J.*, 1946, 1011) described the formation of this acid in 7% yield by the following route :



He did not isolate either of the intermediates, the entire non-volatile fraction from the malonic ester condensation being hydrolysed to a syrupy acid which was pyrolysed at 160—180° to give a non-crystalline product. This was esterified, a small quantity of the methyl ester of (X) and a much larger quantity of a higher-boiling product, formulated as the ester of (XI), being obtained. It was stated that (X) was formed only if the scale of the decarboxylation reaction was small.

This scale-variability seemed surprising and the reaction sequence was therefore reinvestigated. The tetracarboxylate was separated by distillation from much non-volatile material, presumably of the type $[C(CO_2Et)_2 \cdot CH_2 \cdot C \equiv C \cdot CH_2]_n$. A crystalline tetracarboxylic acid was readily obtained which when carefully purified gave at 160° an almost quantitative yield of pure (X), whatever the scale of the experiment. When the crude tetra-acid, containing a trace of mineral acid as a result of the continuous-extraction process necessary for its isolation, was heated at 160° in nitrogen, the decarboxylation product was non-crystalline and gave, on esterification, a main fraction of much higher boiling point than the ester of (X). This had physical properties approximating to those quoted by Johnson for the ester of (XI), but analytical data were in poor agreement with such a constitution, and it was clearly heterogeneous. Presumably acid-catalysed attack by a carboxyl group on the triple bond, giving initially an enol–lactone (cf. the behaviour of pent-4-ynoic acid mentioned above), is involved; Johnson's evidence, *i.e.*, production of some suberic acid by decarboxylation following hydrogenation under vigorous conditions, is compatible with such a hypothesis.

The acid (X), like its analogue hex-4-ynoic acid, underwent isomerisation only under drastic conditions, indeed it was appreciably less reactive, perhaps because of the additional negative charge on the anion. After 16 hours in a 17% solution of potassium hydroxide in ethylene glycol at 167° it gave a 55% yield of deca-3 : 5-dienedioic acid. This high-melting acid, like (X), was readily characterised as a crystalline dimethyl ester.

Experimental

Melting-points were measured on the Kofler block, and ultra-violet and infra-red spectra were normally determined in 95%-alcoholic and carbon tetrachloride solutions, respectively.

Penta-2 : 3-dienedioic Acid (II).—A solution of chromic acid (6N in 12N-sulphuric acid; 11 c.c.) was added to a stirred, cooled solution of 5-hydroxypent-2-ynoic acid (1·9 g.; Haynes and Jones, *J.*, 1946, 954) in acetone (50 c.c.) at 20°. After 2 hr. water was added and the mixture was extracted continuously with ether. Evaporation of the dried extract and crystallisation of the residue from ether–light petroleum (b. p. 40—60°) gave the allenic acid (0·5 g.), m. p. 149—150° undepressed on admixture with a specimen prepared by van der Zanden's method (*loc. cit.*). The methyl ester was prepared with diazomethane; it had b. p. 90° (bath temp.)/0·2 mm., n_D^{19} 1·4853 (Makulec, Malachawski, and Manitus, *Chem. Zentr.*, 1929, 1328, give b. p. 101°/6 mm., n_D^{19} 1·4878).

Hex-3-ynedioic Acid (III).—Chromic acid (as above; 35 c.c.) was added to a stirred, cooled solution of hex-3-yne-1 : 6-diol (3·0 g.) in acetone (100 c.c.) at 20°. After 2 hr. water was added and the product was isolated by continuous extraction with ether. Evaporation and crystallistion of the residue from water gave the *acid* (1·8 g.), m. p. 174—175° (Found: C, 50·85; H, 4·4. $C_6H_6O_4$ requires C, 50·7; H, 4·3%). Light absorption: no maximum above 2000 Å, where ε = 315. The *methyl* ester, prepared with 2·5% sulphuric acid in methanol at 65°, formed needles, m. p. 64—65° (Found: C, 56·45; H, 5·65. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9%).

6-*Hydroxyhex-2-ynoic Acid* (V).—5-2′-Tetrahydropyranyloxy-pent-1-yne (21 g.) in benzene (30 c.c.) was added to a solution of ethylmagnesium bromide in benzene, prepared from magnesium (3·3 g.). The mixture was stirred for 1 hr. at 20° and 1 hr. at 50°, cooled, and poured on to a large excess of solid carbon dioxide in a steel autoclave, which was sealed. After 24 hr., release of excess of carbon dioxide, and cautious decomposition with dilute sulphuric acid gave a benzene layer containing the tetrahydropyranyl ether of the desired acid. Evaporation of the solvent and treatment with sulphuric acid (2N; 400 c.c.) for 24 hr., followed by continuous extraction with ether, and evaporation of the extract, gave a solid residue. Crystallisation from ether–light petroleum yielded 6-*hydroxyhex-2-ynoic acid* (3·0 g.), m. p. 65—66° (Found: C, 56·4; H, 6·35. $C_6H_8O_3$ requires C, 56·2; H, 6·3%). Light absorption: maximum, 2070 Å; ε = 6100. A Nujol mull showed intense infra-red absorption at 2240 cm.$^{-1}$ and other expected frequencies.

Hex-2-ynedioic Acid (VI).—(*a*) Chromic acid (as above; 35 c.c.) was added to a stirred, cooled solution of hex-2-yne-1 : 6-diol (3·0 g.; Paul and Tchelitcheff, *Bull. Soc. chim.*, 1953, 418) in acetone (25 c.c.) below 38° during 20 min. The upper layer was evaporated under reduced pressure, and the residue extracted with tetrahydrofuran (3 × 25 c.c.) at 50°, leaving a residue containing chromium. Evaporation of the tetrahydrofuran gave a solid which was purified by crystallisation from ether–light petroleum, yielding the *acid* (0·7 g.), m. p. 139—140° (Found: C, 51·0; H, 4·55. $C_6H_8O_4$ requires C, 50·7; H, 4·3%). Light absorption: maximum, 2060 Å; $\varepsilon = 5300$. A Nujol mull showed intense absorption at 2250 cm.$^{-1}$.

(*b*) Similar oxidation of 6-hydroxyhex-2-ynoic acid (2·3 g.) with chromic acid (12 c.c.), and crystallisation of the crude product from nitromethane gave the dicarboxylic acid (0·6 g.), m. p. 139—140°, undepressed on admixture with material prepared as above.

Rearrangement of the Hexynedioic Acids.—In trial experiments, a solution of the hexynedioic acid in 9% potassium hydroxide (100 c.c. per g.) was heated to 40° or 103° (under reflux), samples being withdrawn at intervals and added to an excess of sulphuric acid. In this solvent *trans-trans*-muconic acid has $\lambda_{max.}$ 2655 Å, $\varepsilon = 30{,}100$; the samples withdrawn were examined in the region 2300 to 2800 Å, where all absorbed maximally at 2655 Å; the muconic acid content could readily be determined.

In preparative experiments the isomerised acid was isolated by continuous extraction with ether. The muconic acid was identified by conversion into the *trans-trans*-dimethyl ester, m. p. and mixed m. p. 157—158°. No attempt was made to isolate any of the *cis-trans*- or the *cis-cis*-isomer, which might also be present, and since these acids absorb less intensely than the *trans-trans*-isomer (Elvidge, Linstead, Sims, and Orkin, *J.*, 1950, 2238) the yields calculated from spectroscopic data are minimal.

Hept-3-yne-1 : 7-diol.—*5-2′-*Tetrahydropyranyloxy-pent-1-yne (22·0 g.) in benzene (50 c.c.) was added to a solution of ethylmagnesium bromide in benzene, prepared from magnesium (3·5 g.). The mixture was heated to 40° for 1 hr., then cooled and treated with ethylene oxide (20 c.c.); a very viscous complex then separated, stirring becoming impossible. After 3 hr. at 65° the mixture was cooled and treated with dilute sulphuric acid. The ethereal extract of the aqueous phase was added to the benzene layer, and the solvents were removed, leaving the tetrahydropyranyl ether of the desired glycol as an oil. Treatment with methanolic sulphuric acid (4%; 200 c.c.) for 7 hr. at 20°, followed by neutralisation with sodium methoxide and evaporation of the filtrate, gave a residue containing mineral salts. Extraction with ethyl acetate, evaporation, and distillation gave the *glycol* (8·5 g.), b. p. 102—104°/0·05 mm., n_D^{18} 1·4870 (Found: C, 65·85; H, 9·0. $C_7H_{12}O_2$ requires C, 65·6; H, 9·4%). The *bis-3 : 5-dinitrobenzoate*, crystallised from benzene, had m. p. 131—132° (Found: N, 10·6. $C_{21}H_{16}O_{12}N_4$ requires N, 10·8%).

Hept-3-ynedioic Acid (VII).—Chromic acid solution (as above; 31 c.c.) was added to a solution of the above glycol (3·05 g.) in acetone (50 c.c.) at 20° during 30 min. After 2 hr., water was added and the solution was extracted continuously with ether. Evaporation of the ether and recrystallisation of the residue from nitromethane gave *hept-3-ynedioic acid* (0·71 g.), m. p. 155—157° (Found: C, 53·85; H, 5·05%; equiv., 77. $C_7H_8O_4$ requires C, 53·8; H, 5·2%; equiv., 78). Light absorption: no maximum above 2000 Å, where $\varepsilon = 290$.

Tetraethyl Hex-3-yne-1 : 1 : 6 : 6-tetracarboxylate.—1 : 4-Dichlorobut-2-yne (50 g.) was condensed with sodiomalonic ester, prepared from diethyl malonate (215 g.) and sodium (25 g.), by Johnson's method (*loc. cit.*), except that the crude product was distilled directly, giving the *tetracarboxylic* ester (70·1 g.), b. p. 146°/0·05 mm., n_D^{18} 1·4551 (Found: C, 58·65; H, 7·3. $C_{18}H_{26}O_8$ requires C, 58·4; H, 7·1%).

Hex-3-yne-1 : 1 : 6 : 6-tetracarboxylic and -1 : 6-dicarboxylic (*Oct-4-ynedioic*) *Acids.*—The above ester (13 g.) was heated under reflux with potassium hydroxide solution (10%; 100 c.c.) for 16 hr. Acidification, continuous extraction with ether, and evaporation gave a residue (8·8 g.), m. p. 152—158°, which was crystallised from nitromethane to give the pure *tetracarboxylic acid* (7·9 g.), m. p. 163—164° (Found: C, 46·55; H, 4·1; equiv., 64·8. $C_{10}H_{10}O_8$ requires C, 46·55; H, 3·9%; equiv., 64·5). Light absorption: no maximum above 2000 Å, where $\varepsilon = 615$.

The pure tetracarboxylic acid (9·2 g.) was heated to 175° in an atmosphere of nitrogen for 40 min. After the acid had melted and effervesced, the dicarboxylic acid (5·5 g.) solidified and had m. p. 200—206° (Johnson, *loc .cit.*, gives m. p. 208—209°). Light absorption: no maximum above 2000 Å, where $\varepsilon = 320$. Treatment with methanolic sulphuric acid (80 c.c.; 6%) for 5 days at 20° gave the dimethyl ester (5·9 g.), m. p. 28—30° (Johnson, *loc. cit.*, gives m. p. 30—32°).

The tetracarboxylic ester, in carbon tetrachloride, and the tetracarboxylic and dicarboxylic

acids in Nujol mulls, showed no absorption of appreciable intensity in the region 1600—1650 cm.$^{-1}$, characteristic of αβ-ethylenic acids and esters.

Octa-2 : 4-dienedioic Acid.—Oct-4-ynedioic acid (1·5 g.) was heated under reflux with a solution of potassium hydroxide (5 g.) in ethylene glycol (25 c.c.) for 16 hr. Acidification, dilution with water, and continuous extraction with ether, and recrystallisation of the extract from water gave the rearranged *acid* (0·9 g.), m. p. 221—222° (Found : C, 56·7; H, 6·15. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9%). Light absorption : maximum, 2540 Å; ε = 23,700. The *dimethyl* ester was prepared with cold methanolic sulphuric acid; after sublimation and recrystallisation from light petroleum at −70° it had m. p. 37—38° (Found : C, 60·6; H, 7·05. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%). Light absorption : maximum, 2580 Å; ε = 29,400. The acid, examined in a Nujol mull, showed intense bands at 1630 and 1610 cm.$^{-1}$.

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Researches on Acetylenic Compounds. Part XLVIII. The Prototropic Rearrangements of Some Diacetylenic Dicarboxylic Acids.*

By E. R. H. JONES, B. L. SHAW, and M. C. WHITING.

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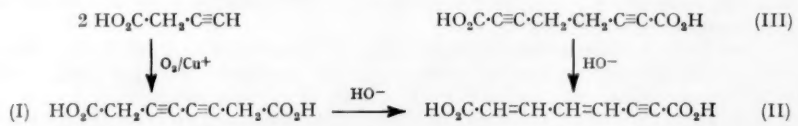
Studies on prototropic isomerisation have been extended to diacetylenic dicarboxylic acids, from which conjugated dienyne- and tetraene-dicarboxylic acids are obtained.

THE preceding paper describes the rearrangements observed when acetylenic dicarboxylic acids are heated in alkaline solutions, a frequent result being the formation of conjugated diene systems. The scope and limitations of this reaction with analogous diacetylenic acids have now been investigated.

Oxidation of octa-3 : 5-diyne-1 : 8-diol with chromic acid gave an acidic product from which it proved impracticable to separate the pure acid (I). Oxidative coupling of but-3-ynoic acid at 35° gave a heterogeneous product, but at 10° an excellent yield of the acid (I) was obtained. Alternatively ethyl but-3-ynoate was coupled to give the ester of (I) in good yield.

The acid (I) rearranged to an isomeric acid (II) in 10% potassium hydroxide solution at 55°. Spectroscopic measurements suggested that the yield was about 60%, but the product was both heterogeneous and unstable, and only 15% of a pure acid, presumably



the *trans-trans*-isomer, could be isolated on crystallisation. It decomposed without melting, but gave a methyl ester, m. p. 114—115°. Alternatively the crude isomerisation product was esterified, giving a complex mixture from which two esters, m. p.s 114—115° and 56—57°, were isolated in low yield by chromatography and fractional crystallisation. From infra-red data these were clearly stereoisomers, and there were indications that the other possible stereoisomers of (II) were present in the crude rearrangement product.

* Part XLVII, preceding paper.

Complete hydrogenation of the rearranged acid gave suberic acid. Of the possible structures (II—VI), (III), (IV), and (V) fail to explain the strong light-absorption band at 2920 Å shown by the rearranged acid ($\varepsilon = 30{,}500$ and 17,500 for the pure material and the crude mixture of stereoisomers, respectively), while the absence of absorption in the infra-red at *ca.* 1970 cm.$^{-1}$ eliminates the allenic structures (IV) and (V). The intense bands near 2195 and 2220 cm.$^{-1}$ shown by the acid and both esters strongly support structure (II) rather than (VI), since the symmetrical environment of the triple bond in

(IV) $HO_2C{\cdot}CH{=}C{=}CH{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CO_2H$ $\qquad$ $HO_2C{\cdot}CH{=}C{=}CH{\cdot}CH{=}C{=}CH{\cdot}CO_2H$ (V)

$HO_2C{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2H$ (VI)

(VI) should lead to an infra-red inactive stretching frequency as in acetylenedicarboxylic acid. An attempt was made to prove structure (II) by indirect hydration; the dimethyl ester was treated with diethylamine, and the adduct (cf. Ruhemann *et al.*, *J.*, 1898, **73**, 723) was hydrolysed with dilute mineral acid (Moureu and Lazennac, *Bull. Soc. chim.*, 1906, **35**, 1190), giving the crystalline hydration product in 50% overall yield. It appeared from its ultra-violet absorption spectrum to exist entirely in the enolic form (VII), and on treatment with concentrated alkali it hydrolysed only to the corresponding acid, instead of undergoing the desired ketonic or acidic fission. As an alternative, the acid (II) was treated with mercuric sulphate and sulphuric acid; hydration was then accompanied by decarboxylation. The resultant keto-acid, (VIII), was smoothly degraded by hypoiodite to iodoform and *trans-trans*-muconic acid, which could only have been derived, ultimately, from (II).

$$MeO_2C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}CO_2Me \xrightarrow[HCl]{NHEt_2;} MeO_2C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}C(OH){=}CH{\cdot}CO_2Me \quad \text{(VII)}$$

$$HO_2C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}CO_2H \xrightarrow{Hg^{++}/H_2SO_4} HO_2C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CO{\cdot}CH_3 \quad \text{(VIII)}$$

The acid (III) (Lespieau, *Ann. Chim.*, 1912, **27**, 137), when treated with 12% potassium hydroxide solution at 65°, similarly gave a solution showing intense absorption at 2920 Å. Isolation of the acidic product gave again apparently a mixture of stereoisomers of (II), although in this case only the methyl ester, m. p. 114—114·5°, could be isolated; the spectroscopic yield of acid was again about 60%, and 25% of the *trans-trans*-isomer could be obtained by recrystallisation. Preparatively this is the best route to (II).

Under comparable conditions both diacetylenic acids (I and III) underwent rearrangement according to a first-order law, the rate constant for (I) being about seven times larger than that for (III). In the second case the sequence of events is fairly obvious; the reaction rate observed is comparable with that of the transformation of pent-2-ynoic into penta-2 : 3-dienoic acid (*J.*, 1954, 3201), and probably corresponds to the slow formation of octa-2 : 3-dien-5-ynedioic acid, which would then more rapidly isomerise to (II), *i.e.* :

$$^-O_2C{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CO_2^- \rightleftharpoons {}^-O_2C{\cdot}CH{=}C{=}CH{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CO_2^-$$

$$\downarrow$$

$$^-O_2C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}CO_2^-$$

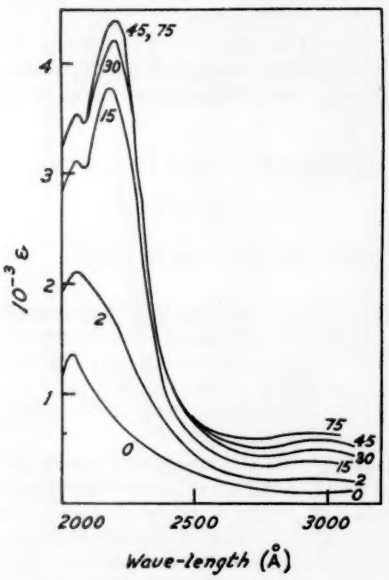
The isomerisation of octa-3 : 5-diyndioic acid (I) must be more complex, however, and attempts were made to detect intermediate products. When it was treated with 10% sodium carbonate solution no alteration in the ultra-violet absorption spectrum was observed at room temperature, but at 62° changes occurred which are illustrated in the Figure. Clearly the slow formation of (II) is preceded by the fairly rapid formation, to equilibrium, of a substance with $\lambda_{max.}$ 2190 Å. The acidic product when isolated at this stage contained much starting material, but the non-crystalline material from the mother-liquors showed

intense absorption at 1970 cm.$^{-1}$ in the infra-red, characteristic of an allenic grouping. This substance must be either (IV) or (V):

$$-O_2C\cdot CH_2\cdot C{\equiv}C\cdot C{\equiv}C\cdot CH_2\cdot CO_2^- \overset{(i)}{\rightleftharpoons} -O_2C\cdot CH{=}C{=}CH\cdot C{\equiv}C\cdot CH_2\cdot CO_2^-$$

$$-O_2C\cdot CH{=}CH\cdot CH{=}CH\cdot C{\equiv}C\cdot CO_2^- \overset{(iii)}{\longleftarrow} -O_2C\cdot CH{=}C{=}CH\cdot CH{=}C{=}CH\cdot CO_2^- \quad (ii)$$

By analogy with simpler systems (preceding papers and unpublished work) it would be expected that reaction (ii) would be somewhat, but not greatly, slower than (i), with (iii) slower still; also that the anion of (V) would predominate over that of (IV) at equilibrium. The equilibrium between these anions and that of (I), however, might well favour the latter, in which the presumably strong interaction of two conjugated acetylenic linkages is possible—a factor not involved in the related equilibria involving but-3-ynoic and buta-2 : 3-dienoic anions. If the light absorption at 2190 Å is attributed essentially to (V), for which the predicted spectrum would be a composite of butadiene and (acrylic acid × 2), but rather more intense (Celmer and Solomons, *J. Amer. Chem. Soc.*, 1953, **75**, 1372, and unpublished work from these laboratories), we may assume $\varepsilon = 50{,}000$, approximately, and deduce that at equilibrium about 10% of the anion of (V) is present, together with a smaller amount of the anion of (IV), the remainder being the diacetylenic isomer.



Figures indicate timei n minutes.

Preliminary experiments with the dimethyl ester of (I) and 1% aqueous potassium carbonate or 1% triethylamine in aqueous dioxan revealed a similar but less favourable situation. The formation of an initial absorption band at *ca.* 2200 Å was followed by a rapid increase in optical density at 2500—3100 Å and obvious darkening. When the reaction was interrupted, products showing intense infra-red absorption bands at 1960 cm.$^{-1}$ indicated the presence of allenes.

The diacetylenic acid (IX) was prepared by oxidative coupling of pent-4-ynoic acid (Eglinton and Whiting, *J.*, 1953, 3052). In boiling 10% potassium hydroxide it gave a 20% yield (spectroscopic) of deca-2 : 4 : 6 : 8-tetraenedioic acid (X); this is an attractive preparative method, of added interest since this acid is a component of the antibiotic fumagillin (Shenck, Hargie, Tarbell, and Hoffman, *J. Amer. Chem. Soc.*, 1953, **75**, 2274). As an alternative route, the acid (XI) was prepared by carboxylation of octa-1 : 7-diyne. Isomerisation under varied conditions failed to reveal the unmistakable spectrum of (X) but a sparingly soluble acid, clearly (XII), was obtained in small yield. No other compounds could be isolated from the experiments with either (IX) or (XI), indicating the relative importance of addition of HO^-, followed by fission, in these cases; both $-C{\equiv}C-C{\equiv}C-$ and $-C{\equiv}C-CO_2^-$ systems are known to undergo addition reactions with, for

$$\text{(IX)}\quad HO_2C\cdot CH_2\cdot CH_2\cdot C{\equiv}C\cdot C{\equiv}C\cdot CH_2\cdot CH_2\cdot CO_2H \longrightarrow HO_2C\cdot[CH{=}CH]_4\cdot CO_2H \quad \text{(X)}$$

$$\underset{\text{(XI)}}{HO_2C\cdot C{\equiv}C\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot C{\equiv}C\cdot CO_2H} \longrightarrow \underset{\text{(XII)}}{HO_2C\cdot CH_2\cdot C{\equiv}C\cdot CH_2\cdot CH_2\cdot C{\equiv}C\cdot CH_2\cdot CO_2H}$$

example, EtO^- with relative ease. Thus the presence of αβ- (or βγ-) acetylenic linkages in particular is undesirable if a prototropic rearrangement leading to a polyene-acid is required.

Ultra-violet light-absorption data are summarised below (λ are recorded in Å):

Substance	$\lambda_{max.}$	$10^{-3}\varepsilon$	$\lambda_{max.}$	$10^{-3}\varepsilon$	$\lambda_{max.}$	$10^{-3}\varepsilon$	$\lambda_{max.}$	$10^{-3}\varepsilon$
I	2080	1·3	2300 *	0·62	2400	0·54	2540	0·32
I; Me ester	2150	1·7	—	—	2400	0·72	2540	0·32
I; Et ester	2150	2·0	—	—	2400	0·72	2540	0·40
IX	—	—	2250	0·47	2380	0·42	2530	0·25
IX; Me ester	—	—	2250	0·45	2390	0·36	2530	0·21
III	2060	11·7						
III; Me ester	2070	12·4						
XI	2070	13·0						
XI; Me ester	2080	12·7						
II	—	—	—	—	2920	30·5		
II; Me ester [a]	2100	6·1	—	—	2920	37·5	3040 *	29
II; Me ester [b]	2100	7·0	—	—	2930	30	3060 *	23
VII	2320	3·4	3380	39·5				
VII; in NaOH	2630	6·0	4160	35				
VIII	2720	23						
VIII [c]	2620	16·3	3020	12·3	3915	38		

* Inflexion. [a] M. p. 115°. [b] M. p. 57°. [c] Methyl ester 2 : 4-dinitrophenylhydrazone.

The diacetylenic acid (I) and its esters show appreciable interaction between the methoxycarbonyl groupings and the unsaturated system, resulting in the appearance of a new maximum near 2100 Å, but not in the hyperchromic and bathochromic displacements characteristic of hyperconjugative auxochromes like hydroxyl or chloro (cf. Armitage and Whiting, *J.*, 1952, 2005). Data for the methyl ester of (X) are included in the next paper; infra-red spectra are summarised below, except for those of the stereoisomeric esters of (II), for which extensive comparisons with model compounds are required to establish the configurations of the ethylenic linkages.

Experimental

Melting-points were determined on the Kofler block. Ultra-violet spectra were obtained with a Unicam SP500 Spectrophotometer known to give results little affected by scattered light even at 2000—2150 Å when appropriate precautions were taken, low optical densities and 1-mm. cells being used as a matter of routine in this region. Infra-red spectra were recorded with a Perkin-Elmer Model 21 Spectrophotometer. "Light petroleum" refers to the fraction, b. p. 40—60°, unless otherwise stated.

Octa-3 : 5-diynedioic Acid (I).—But-3-ynoic acid (2·1 g.), ammonium chloride (10 g.), cuprous chloride (6 g.), and water (30 c.c.) were shaken in oxygen until absorption was complete; external cooling to *ca.* 10° was necessary to prevent darkening and a reduction in yield. 3N-Hydrochloric acid was added to dissolve copper salts, and the suspension was extracted continuously with ether. Evaporation gave the essentially pure *acid* in quantitative yield; crystallisation from water gave plates, m. p. 210° (decomp.) (Found: C, 57·6; H, 3·7. $C_8H_6O_4$ requires C, 57·85; H, 3·65%). Hydrogenation over platinum (uptake 3·8 mols.) gave suberic acid in 80% yield. The *methyl* ester was obtained by treating the diacetylenic acid with 5% sulphuric acid in methanol for 14 days at 18°; it had b. p. 130°(bath temp.)/1 mm., m. p. 53° (Found: C, 62·0; H, 5·3. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%).

Diethyl Octa-3 : 5-diynedioate.—This *ester* was obtained in 63% yield by oxidative coupling of ethyl but-3-ynoate, or in 80% yield from the diacid, as long needles, m. p. 60°, from aqueous ethanol (Found: C, 64·8; H, 6·25. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%).

Isomerisation of Octa-3 : 5-diynedioic Acid (I).—A solution of the acid (2·00 g.) in potassium hydroxide solution (10%; 60 c.c.) was heated to 55° for 1 hr., the intensity of absorption at 2920 Å having then become constant. Cooling and acidification gave a precipitate (1·51 g.) (Found: equiv., 93·0. $C_8H_6O_4$ requires equiv., 83·0), $\varepsilon_{max.}$ at 2910 Å = 17,500. Continuous extraction of the filtrate with ether gave a syrup (0·35 g.) without significant absorption in the ultra-violet.

The crude *acid* (1·26 g.) was treated with the theoretical quantity of diazomethane in ether. When the colour had disappeared, an acidic fraction (260 mg.; $\lambda_{max.}$ 2900 Å, ε = 10,700) and a neutral fraction (967 mg.) were separated. Chromatography on deactivated alumina from benzene gave (*a*) 216 mg. of esters, m. p. 23—45°, $\lambda_{max.}$ 2930, ε = 25,600, (*b*) 341 mg. of higher-melting and more intensely-absorbing fractions, and (*c*) gummy material eluted with chloroform. Fractions (*a*) and (*b*) still behaved as mixtures of closely-similar substances, but by further

chromatography followed by two crystallisations from light petroleum fraction (*a*) yielded *dimethyl octa*-trans-2 : cis-4-*dien*-6-*ynedioate* (42 mg.) as plates, m. p. 56—57° (Found : C, 61·85; H, 5·15. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%). Fraction (*b*) gave the ester, m. p. 114—115°, described below, in small yield on similar treatment.

In a similar experiment the crude acid (4·0 g.) was crystallised from water, the only satisfactory solvent, giving *octa*-trans-2 : trans-4-*dien*-6-*ynedioic acid* (II) (0·81 g.) as microscopic plates which decomposed above 150° without melting (Found : C, 57·6; H, 3·7. $C_8H_6O_4$ requires C, 57·85; H, 3·65%). This recovery varied little in several experiments; no homogeneous product could be isolated from the mother-liquors. Hydrogenation (uptake 3·85 mols.) gave suberic acid in almost quantitative yield. The *dimethyl* ester was obtained in 45% yield from the recrystallised acid, separating in prisms, m. p. 114—115°, from 10% sulphuric acid in methanol during 14 days at room temperature (Found : C, 62·1; H, 5·4. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%).

Isomerisation of Octa-2 : 6-*diynedioic Acid*.—This acid (2·0 g.), potassium hydroxide (6·0 g.), and water (50 c.c.) were heated to 65° for 1·5 hr. Acidification and isolation with ether gave a crude product (1·8 g.) which was crystallised from water, giving octa-2 : 4-dien-6-ynedioic acid (0·50 g.); this had ultra-violet light-absorption properties identical with those of the acid obtained as above. Esterification gave the same methyl ester, m. p. 114—115°.

Dimethyl 3-*Hydroxyocta*-2 : 4 : 6-*trienedioate* (VII).—Dimethyl octa-2 : 4-dien-6-ynedioate, m. p. 114—115° (170 mg.), chloroform (4 c.c.), and diethylamine (0·2 c.c.) were set aside for 16 hr. Evaporation of the solvent below 20° gave an oil which was shaken with 5% hydrochloric acid (10 c.c.) for 40 min. Isolation with ether and crystallisation from aqueous ethanol gave the *hydroxy*-ester (92 mg.), m. p. 126·5—128° (Found : C, 56·7; H, 5·75. $C_{10}H_{12}O_5$ requires C, 56·6; H, 5·7%); its infra-red spectrum in carbon tetrachloride included bands at 3465 (O–H), 1720, 1705 (C=O), and 1612 cm.$^{-1}$ (C=C).

6-*Oxohepta*-2 : 4-*dienoic Acid*.—Octa-2 : 4-dien-6-ynedioic acid (320 mg.), mercuric sulphate (*ca.* 10 mg.), and sulphuric acid (2·5N; 25 c.c.) were heated to 95° for 10 min. Isolation of the acidic fraction with ether gave a solid which was extracted with hot benzene; evaporation of this solution and crystallisation gave the *keto-acid* (177 mg.) as needles, m. p. 140—142° (Found : C, 59·85; H, 5·8. $C_7H_8O_3$ requires C, 60·0; H, 5·75%). The 2 : 4-*dinitrophenylhydrazone* of the methyl ester formed scarlet needles, m. p. 214—218° (Found : C, 50·7; H, 4·35; N, 16·5. $C_{14}H_{14}O_6N_4$ requires C, 50·3; H, 4·2; N, 16·75%).

Muconic Acid.—The keto-acid (95 mg.), sodium hydroxide solution (5%; 4 c.c.), and potassium iodide (700 mg.) were treated with 12% sodium hypochlorite solution at 20° until precipitation of iodoform (170 mg., 66%) ceased. Acidification gave *trans-trans*-muconic acid (39 mg., 40%), m. p. *ca.* 300°, $\lambda_{max.}$ 2610 Å, $\varepsilon = 25{,}000$. Esterification gave the dimethyl ester, m. p. and mixed m. p. 157—158°.

Deca-4 : 6-*diynedioic Acid* (IX).—Pent-4-ynoic acid (2·5 g.), cuprous chloride (6·0 g.), ammonium chloride (10 g.), and water (33 c.c.) were shaken in oxygen until uptake was complete. Addition of 5N-hydrochloric acid dissolved the copper salts, and filtration gave the insoluble diacetylenic *acid*, which separated from hot water as microscopic needles which decomposed without melting above 220° (yield 1·65 g.) (Found : C, 61·65; H, 5·3. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%). Hydrogenation (uptake 4·15 equiv.) gave sebacic acid, m. p. and mixed m. p. 132·5—133°, in quantitative yield. The dimethyl ester was obtained at 20° with 9% methanolic sulphuric acid for 14 days (yield 63%); it formed leaflets, m. p. 36° (Found : C, 64·85; H, 6·55. Calc. for $C_{12}H_{14}O_4$: C, 64·85; H, 6·35%). Christiansen and Sörensen (*Acta Chem. Scand.*, 1952, **6**, 893) give m. p. 37·5°, but their specimen, from published ultra-violet data, must have contained a more highly unsaturated impurity.

Dimethyl Deca-2 : 4 : 6 : 8-*tetraenedioate* (*Diester of* X).—The above acid (600 mg.) was heated in potassium hydroxide solution (10%; 20 c.c.) under reflux for 3 hr. Acidification gave the rearranged acid which was separated by centrifugation (320 mg.); it could not easily be purified, and was therefore heated with thionyl chloride (5·5 c.c.) for 1 hr. Removal of excess of reagent gave the crystalline dichloride which was treated with methanol. After sublimation at 150°/0·02 mm. and crystallisation from *cyclo*hexanol the ester (110 mg.) had m. p. 209—212° (Kuhn and Grundmann, *Ber.*, 1936, **69**, 1757, give m. p. 212°) (Found : C, 64·7; H, 6·4. Calc. for $C_{12}H_{14}O_4$: C, 64·85; H, 6·35%).

Deca-2 : 8-*diynedioic Acid* (XI).—A solution of ethylmagnesium bromide, prepared in ether from magnesium (2·64 g.), was treated with octa-1 : 7-diyne (5·3 g.), and the mixture was heated under reflux for 1·5 hr. The suspension of the Grignard complex was transferred to a 250-c.c. autoclave containing solid carbon dioxide (*ca.* 100 g.). After 18 hr. excess of carbon dioxide

was released, sulphuric acid was added, and the solution was extracted continuously with ether. Evaporation of the dried extract and crystallisation of the residue from nitromethane gave the *acid* (6·2 g., 67%) as plates, m. p. 159—161° (Found: C, 61·95; H, 5·3. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%). Its infra-red spectrum included an intense band at 2236 cm.$^{-1}$ (–C≡C–, conjugated). Hydrogenation (uptake 4·2 equiv.) gave sebacic acid, m. p. and mixed m. p. 133°. The *methyl* ester, prepared with methanolic sulphuric acid at room temperature, formed needles, m. p. 35·5—36·5°, from light petroleum (b. p. 30—40°) (Found: C, 65·0; H, 6·45. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%).

Deca-3 : 7-diynedioic Acid (XII).—The above acid (500 mg.) and potassium hydroxide solution (15%; 20 c.c.) were heated under reflux for 20 min.; isolation of the acidic fraction gave a syrup which was treated with ether, the isomeric *acid* (49 mg.) separating. Crystallisation from nitromethane gave the pure product, m. p. 170—183° (decomp.) (Found: C, 62·0; H, 5·35. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%). The *dimethyl* ester was prepared with diazomethane. After sublimation and crystallisation from light petroleum, then twice from aqueous methanol the yield was 54% of needles, m. p. 40·5—41° (Found: C, 65·0; H, 6·35. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%). Both acid and ester showed only weak absorption at *ca.* 2200 cm.$^{-1}$. Neither absorbed intensely in the ultra-violet (cf. deca-2 : 7-diynedioic acid, above), ε being about 850 at 2020 Å in each case and falling steeply at longer wave-lengths.

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Researches on Polyenes. Part I. The Synthesis of Corticrocin.

By B. L. SHAW and M. C. WHITING.

[Reprint Order No. 5307]

The constitution (I*a*; $n = 6$), proposed for the fungus pigment corticrocin, has been confirmed by synthesis.

A PIGMENT, "corticrocin," was recently isolated from the mycorrhizal fungus *Corticium croceum* Bres. by Erdtman (*Acta Chem. Scand.*, 1948, **2**, 209), and shown to be the unbranched polyenedicarboxylic acid (I*a*; $n = 6$). The immediate homologues (I*a*; $n = 5$ and 7) of this acid had been prepared by Kuhn and Grundmann (*Ber.*, 1936, **69**, 1979; 1937, **70**, 1318) from octa-2 : 4 : 6-trienal and dodeca-2 : 4 : 6 : 8 : 10-pentaenal, respectively, by long routes and in low overall yields. Deca-2 : 4 : 6 : 8-tetraenal is much less accessible than these aldehydes (Kuhn and Hoffer, *Ber.*, 1930, **63**, 2164; Blout and Fields, *J. Amer. Chem. Soc.*, 1948, **70**, 189); thus the analogous synthesis of (I*a*; $n = 6$) would in practice be tedious and difficult.

In contrast, rearrangements of the type described in the preceding papers offered a convenient route to (I*a*; $n = 6$), provided that a straight-chain C_{14} αω-dicarboxylic acid with six units of unsaturation, and without αβ- or βγ-acetylenic linkages, could be obtained. Symmetrical acids are relatively accessible *via* the excellent oxidative coupling reaction of ω-acetylenic compounds, and two such acids, (II) and (III), were considered. The former was expected to give a higher yield of the polyene acid (I*a*) than would (III), with which the first step requires attack on a hydrogen atom which is only weakly activated, and the synthesis of (II) was therefore attempted first.

$RO_2C{\cdot}[CH{=}CH]_n{\cdot}CO_2R$ (I; *a*, R = H; *b*, R = Me)

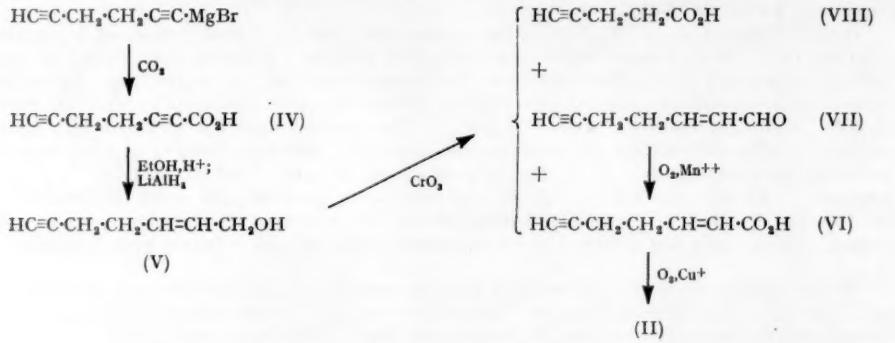
$(C{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}CH{=}CH{\cdot}CO_2H)_2$ (II)

$(C{\equiv}C{\cdot}CH{=}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H)_2$ (III)

The obvious route to (II) involves condensation of pent-4-ynal with malonic acid, followed by decarboxylation and coupling. Unfortunately the direct oxidation of pent-4-yn-1-ol with chromic acid did not give an appreciable quantity of the acetylenic aldehyde

under the conditions tried. The corresponding nitrile was readily obtained from but-3-ynyl toluene-*p*-sulphonate, but reduction with stannous chloride proved unsuccessful.

During earlier work (preceding paper) the carboxylation of hexa-1 : 5-diynylenedimagnesium bromide (Lespieau, *Ann. Chim.*, 1912, **27**, 137) was repeated, and a small quantity of a by-product, hepta-2 : 6-diynoic acid (IV), was isolated. The monobromomagnesium derivative of the hydrocarbon gave 18% of this acid, together with much of the



symmetrical product; no doubt this yield could be improved. Preferential reduction of the αβ-acetylenic linkage took place when its ester was treated with lithium aluminium hydride (see Bates, Jones, and Whiting, *J.*, 1954, 1854, and references cited there), giving hept-2-en-6-yn-1-ol (V) in excellent yield. Subsequent oxidation with chromic acid gave consistently poor (~10%) yields of the desired hept-2-en-6-ynoic acid (VI), but provided much more of the corresponding aldehyde (VII) under milder conditions. When (VII) was shaken with oxygen in the presence of manganese acetate (cf. Owen, *J.*, 1943, 463) a fair yield of the desired acid was obtained.

Oxidative coupling of the acid (VI) (cf. Armitage, Cook, Entwistle, Jones, and Whiting, *J.*, 1952, 1998) gave an almost quantitative yield of (II). This was heated with potassium hydroxide solution, and light-absorption maxima corresponding to those reported by Erdtman (*loc. cit.*) for corticrocin in alkaline solution were soon detected. After selection of optimal conditions (boiling 20% potassium hydroxide; the spectroscopic yield was subsequently estimated as 15%) the reaction was effected on a preparative scale. The crystalline potassium salt then separated even from the boiling solution, and was decomposed giving (I*a*; $n = 6$) in 11% yield. This high-melting and almost insoluble acid was characterised by conversion *via* the acid chloride into the dimethyl ester, m. p. 227—228·5° undepressed on admixture with the ester of natural corticrocin which was kindly supplied by Professor Erdtman.

The ultra-violet absorption spectrum of the product closely resembled that published by Erdtman (*loc. cit.*), but the extinction coefficients at the highest maxima were higher by up to 10%. A redetermination of the spectrum of the natural product gave results identical, within experimental error, with those obtained for the synthetic ester; Professor Erdtman has informed us that the optical densities actually recorded for the natural substance were in the range 1—1·5, where the Beckman instrument would be less accurate than usual.

As a final proof of identity infra-red spectra of the natural and synthetic esters were determined in Nujol. The results were strikingly different, showing respectively one band at 1710 cm.$^{-1}$ and a doublet at 1710 and 1720 cm.$^{-1}$, with other less obvious discrepancies. The explanation proved to be the dimorphism of this ester, which Erdtman had already observed (*loc. cit.*). When the two esters were recrystallised from acetic acid under similar conditions, spectra showing both bands, and otherwise identical, were obtained.

Erdtman concluded tentatively (*loc. cit.*) that corticrocin was an all-*trans*-compound (in contrast to the isoprenoid polyenedicarboxylic ester, bixin), basing his conclusion on the increase in the intensity of light absorption at short wave-lengths when the ester was

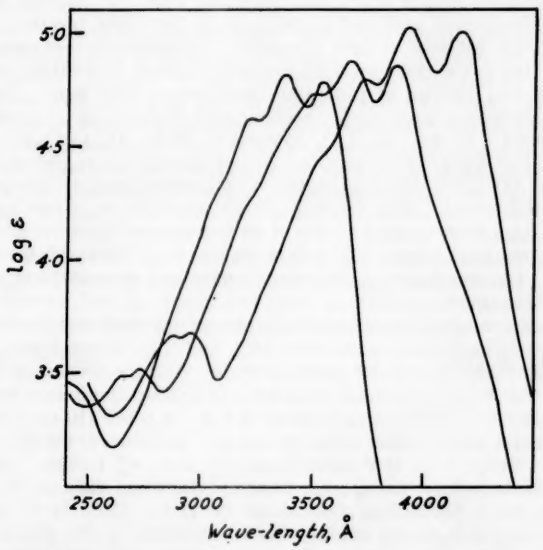
equilibrated with its stereoisomerides by illumination in the presence of iodine. The synthetic ester reproduced this behaviour. The method of synthesis would clearly be expected to give, at least predominantly, the most stable or all-*trans*-isomer; indeed, the advantage in energy of the all-*trans*-isomer in alkaline solution must be a little greater than usual among polyenes, since in it the two $-CO_2^-$ groups are farthest apart. The infra-red spectrum of the methyl ester provides additional confirmation, since strong absorption at 1023 cm.$^{-1}$ (conjugated *trans*-CH=CH–) was unaccompanied by appreciable absorption in the 700—850 cm.$^{-1}$ region where conjugated *cis*-1 : 2-disubstituted ethylenes usually absorb.

In an early experiment a specimen of hept-2-en-6-ynoic acid (VI), prepared by oxidation of the corresponding alcohol, was coupled after only perfunctory purification. After

Absorption Spectra of Esters (I*b*) *in Chloroform.*

$n = 4$		$n = 5$ †		$n = 6$	
$\lambda_{max.}$, Å	$10^{-3}\,\varepsilon$	$\lambda_{max.}$, Å	$10^{-3}\,\varepsilon$	$\lambda_{max.}$, Å	$10^{-3}\,\varepsilon$
3540	60·5	3880	72	4165	103
3370	64·6	3670	74	3935	107
3225	42·2	3500	53	3735	67
		2730	3·3	3560 *	32
		2660 *	3·1	2955	4·8
				2870	4·6

* Inflexion. † Containing *ca.* 7% of (I*b*, $n = 6$), on spectroscopic data.



alkaline isomerisation the insoluble potassium salt was acidified, and the polyene-acid converted *via* the acid chloride into the methyl ester. This was heterogeneous and on chromatographic separation gave, in addition to (I*b*; $n = 6$), an ester which showed an ultra-violet absorption spectrum similar to those of the esters (I*b*; $n = 4$ and 6), and exactly intermediate between them (see Figure). Clearly it must have been (I*b*; $n = 5$), which could have been formed by oxidative fission of hept-2-en-6-yn-1-ol at the ethylenic linkage (much more susceptible to electrophilic attack than the acetylenic bond), followed by cross-coupling of the resultant pent-4-ynoic acid (VIII) with (VI) to give the acid (IX) :

$$\text{(VI)} + \text{(VIII)} \xrightarrow{O_2,Cu^+} HO_2C{\cdot}CH{=}CH{\cdot}CH_2{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H\ \text{(IX)} \xrightarrow{HO^-} \text{(I}a\text{; } n = 5)$$

Since the publication of our preliminary communication (*Chem. and Ind.*, 1953, 409), Weedon has effected a very similar synthesis of corticrocin, involving alkaline hydrolysis and rearrangement of an ester closely related to (III) (*ibid.*, p. 1388).

Experimental

Ultra-violet and infra-red spectra were obtained, in 95% ethanol and carbon tetrachloride unless otherwise stated, with a Unicam SP 500 and a Perkin-Elmer Model 21 spectrophotometer, respectively. "Light petroleum" implies the fraction, b. p. 40—60°; melting points were determined on the Kofler block.

4-Cyanobut-1-yne.—But-3-yn-1-yl toluene-*p*-sulphonate (Eglinton and Whiting, *J.*, 1950, 3650; 12 g.) was added to a solution of potassium cyanide (32·5 g.) in water (20 c.c.) and methanol (200 c.c.). The mixture was heated under reflux for 22 hr., cooled, and filtered; the precipitate was washed with methanol. Removal of most of the methanol by distillation through a short Dufton column, dilution, and extraction with ether, gave a persistent emulsion, easily broken by acidification; distillation of the neutral fraction then gave the *nitrile* (19·7 g., 50%), b. p. 79°/35 mm., n_D^{22} 1·4367 (Found: N, 17·2. C_5H_5N requires N, 17·7%). The expected infra-red maxima at 3275 and 2252 cm.$^{-1}$ (C≡N) were observed, the 1600—1750 cm.$^{-1}$ region being almost free from absorption bands.

Hepta-2:6-diynoic Acid (IV).—Hexa-1:5-diyne (7·8 g.) was added to a solution of ethylmagnesium bromide, prepared in ether from magnesium (2·7 g.), and the mixture heated under reflux for 2 hr. The suspension was transferred to a steel autoclave containing solid carbon dioxide (*ca.* 100 g.); after 24 hr. the complex was decomposed with dilute sulphuric acid, and the aqueous phase thoroughly extracted with ether. Evaporation of the ethereal solutions gave a semi-solid residue which was triturated with cold benzene, giving an insoluble residue of octa-2:6-diynedioic acid (3·7 g., 22%), m. p. 189—190° (decomp.) after recrystallisation [Lespieau, *loc. cit.*, gives m. p. 190° (decomp.)]. The filtrate was extracted with sodium carbonate solution, and the extract acidified and re-extracted with ether; evaporation gave a liquid residue which was distilled at 125—140° (bath temp.)/0·02 mm. Crystallisation of the distillate from light petroleum gave the diacetylenic *acid* (2·15 g.; 18%) as needles, m. p. 52·5—53·5° (Found: C, 68·7; H, 4·9. $C_7H_6O_2$ requires C, 68·8; H, 4·95%). Light absorption: maximum, 2060 Å; ε = 6200. The infra-red absorption spectrum included intense bands at 3290 and 2248 cm.$^{-1}$ (H–C≡C– and conjugated –C≡C–, respectively). Hydrogenation (uptake 3·9 equiv.) gave heptanoic acid, characterised as heptanoamide, m. p. and mixed m. p. 93—95°. The *ethyl* ester, obtained in 90% yield by use of 10% ethanolic sulphuric acid at 20° for 6 days, had b. p. 90° (bath temp.)/1·5 mm., $n_D^{17·5}$ 1·4718 (Found: C, 71·95; H, 6·7. $C_9H_{10}O_2$ requires C, 72·0; H, 6·7%). The ester had $\lambda_{max.}$ 2080 Å, ε = 6950, and showed the expected intense bands at 3295 cm.$^{-1}$ and 2242 cm.$^{-1}$.

When the bis-bromomagnesium derivative was carboxylated under similar conditions the yields of di- and mono-carboxylic acids were 44% and 7%, respectively. The use of tetrahydrofuran in place of ether as solvent would probably afford a considerably increased yield.

Hept-2-en-6-yn-1-ol (V).—To a stirred suspension of lithium aluminium hydride (5·0 g.; 70% purity) in ether (240 c.c.), ethyl heptadiynoate (3·9 g.) in ether (10 c.c.) was added, and the mixture was stirred and heated under reflux for 4·5 hr. Addition of ice and sulphuric acid gave the alcohol (2·65 g., 94%), b. p. 106° (bath temp.)/14 mm., n_D^{20} 1·4739. Analytical data were inconsistent and unsatisfactory, but intense bands at 3290 and 2224 cm.$^{-1}$, and weaker bands at 3605 and 1678 cm.$^{-1}$ (stretching frequencies of H–C≡, C≡C, H–O, and *trans*-CH=CH– groupings, respectively) adequately confirm the constitution of the product, which was free from carbonyl compounds. An *α-naphthylurethane* was readily obtained as matted needles, m. p. 101—102° (Found: C, 77·65; H, 6·2. $C_{18}H_{17}O_2N$ requires C, 77·4; H, 6·15%).

Hept-2-en-6-ynoic Acid (VI).—(*a*) The above alcohol (4·35 g.) in acetone (26·5 c.c.) was treated with a solution of chromic acid (6N) in 12N-sulphuric acid (26·5 c.c.) at 20° with stirring, which was continued for a further 2 hr. After 18 hr. water was added and the acidic and neutral fractions were separated. The former gave the *acid* (550 mg., 11%) as plates, m. p. 82—83°, on crystallisation from water (Found: C, 67·55; H, 6·55. $C_7H_8O_2$ requires C, 67·75; H, 6·5%). Light absorption: maximum, 2080 Å; ε = 12,000; and strong bands at 3297 (H–C≡) and 1654 cm.$^{-1}$ (CH=CH, conjugated), and in regions typical of carboxylic acids. The neutral fraction was distilled giving *hept-2-en-6-ynal* (2·93 g., 69%), b. p. 90°(bath temp.)/10 mm., n_D^{20} 1·4838. Light absorption: maximum, 2200 Å; ε = 16,000; and prominent infra-red bands at 3290, 1697, and 1632 cm.$^{-1}$. The aldehyde absorbed oxygen rapidly, and was therefore

analysed as the *semicarbazone* (plates; m. p. 185—186°; from ethanol) (Found: C, 58·15; H, 6·85. $C_8H_{11}ON_3$ requires C, 58·15; H, 6·7%). Light absorption: maximum, 2470 Å; $\varepsilon = 24{,}000$.

(*b*) The above aldehyde (2·9 g.) was dissolved in light petroleum (b. p. 60—80°; 40 c.c.) and shaken in oxygen in the presence of manganese acetate (5 mg.). After 6 days the uptake was 275 c.c. and absorption had ceased. Isolation of the acidic fraction and crystallisation from water gave the acid (970 mg.; 30%), m. p. 82—83°.

Tetradeca-2 : 12-diene-6 : 8-diynedioic Acid (II).—The above acid (650 mg.), cuprous chloride (2 g.), ammonium chloride (3·5 g.), water (20 c.c.), and acetone (20 c.c.) were shaken in oxygen until uptake (*ca.* 250 c.c.) was complete. Acetone was removed under reduced pressure, and water (40 c.c.) and syrupy phosphoric acid (10 c.c.) were added; copper salts then dissolved and the dicarboxylic acid was precipitated. Filtration, extraction of the residue with sodium hydroxide, and acidification of the filtered extract gave the pure *acid* (582 mg., 90%), which formed needles from acetic acid, decomp. above 150° (Found: C, 68·2; H, 5·6. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7%). Light absorption: maxima, 2070 and 2530 Å; $\varepsilon = 25{,}000$ and 800, respectively; inflexion, 2400 Å; $\varepsilon = 1550$; and a strong infra-red band at 1648 cm.$^{-1}$. The *dimethyl* ester, obtained in 60% yield, formed plates, m. p. 85—86°, from light petroleum (b. p. 80—100°) (Found: C, 69·95; H, 6·6. $C_{16}H_{18}O_4$ requires C, 70·05; H, 6·6%), and had $\lambda_{max.}$ 2070 and 2530 Å, $\varepsilon = 25{,}000$ and 820, respectively.

Tetradeca-2 : 4 : 6 : 8 : 10 : 12-hexaenedioic Acid (*Corticrocin*) (I*a*; $n = 6$).—The diacetylenic acid (586 mg.) and aqueous potassium hydroxide solution (20%; 30 c.c.) were heated under reflux for 1·5 hr. Golden plates began to separate after 5 min.; these were collected when the solution was still warm, washed with 20% potassium hydroxide solution, and dissolved in hot water containing a little sodium hydroxide. The filtered solution was acidified and centrifuged, giving the acid (66 mg.) as an orange-brown powder which decomposed near 300° without melting and proved to be insoluble in all solvents tried. The acid (20 mg.) was heated under reflux with thionyl chloride (2 c.c.) until it dissolved completely (1·5 hr.), and excess of the chloride was removed under reduced pressure, giving the crude acid chloride as a scarlet solid. Dry methanol was then added, and after 1 hr. the surplus was removed; sublimation of the residue at 160°/10^{-4} mm. gave the dimethyl ester (15 mg.), m. p. 209—218°, raised to 227·5—228·5° by crystallisation from glacial acetic acid (yield 9 mg.). The corrected melting-point in an open capillary was 229—230°; no depression was observed on admixture with a specimen of corticrocin dimethyl ester kindly provided by Professor Erdtman (Found: C, 69·9; H, 6·75. Calc. for $C_{16}H_{18}O_4$: C, 70·05; H, 6·6%).

The authors thank Professor E. R. H. Jones, F.R.S., for his interest. They are indebted to the Department of Scientific and Industrial Research for a maintenance grant (B. L. S.); and to Messrs. E. S. Morton and H. Swift, and Miss W. Peadon and Miss J. Shallcross, for microanalyses and infra-red spectroscopic measurements, respectively.

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Dipole Moments of the Lower Dialkyl Alkylphosphonates.

By GENNADY M. KOSOLAPOFF.

[Reprint Order No. 5333.]

The calculation of dipole moments of several lower members of the dialkyl alkylphosphonate series was made from the determinations on the pure liquids, of the dielectric constants of these esters. The values of the dipole moments obtained through the use of the empirical formula proposed by Buckingham and Le Fèvre seem to indicate a low probability of the " folded structure " of such esters, which has been proposed by other workers to explain deviations found among the parachor values in this series of substances.

THERE is a scarcity of experimental data on the dipole moments of esters of aliphatic phosphonic acids. Until a recent publication by the author (*J. Amer. Chem. Soc.*, 1954, **76**, 615) for some diethyl esters of the higher alkylphosphonic acids, the only other determinations were those by Arbuzov and Rakov (*Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1950, 237) with five substances in which all three aliphatic radicals (methyl, ethyl, propyl, *iso*propyl, and butyl) were identical in each ester. Their results on solutions in various solvents were converted into the calculated dipole-moment data by extrapolation. The five esters gave extremely close grouping of the dipole moments (2·86—2·92 D), which seems to indicate a lack of dependence of the resultant moment on molecular constitution.

Since it is well-substantiated that the dipole moments of solute molecules obtained by translation of dielectric-constant data for their solutions often deviate considerably from the " true " values obtainable from measurements in the gaseous state, it was felt that dielectric data obtained for the pure liquids may be at least as useful in calculations of dipole moments as those data for solutions. The same idea has been explored recently by many workers and has resulted in several formulæ of both the theoretically derived and the empirical type. Kosolapoff (*loc. cit.*) used the Onsager formula for computation of dipole moments from dielectric data on the higher diethyl alkylphosphonates. This formula, *viz.*,

$$\mu^2 = \frac{9kTM}{4\pi Nd} \times \frac{(\varepsilon - n^2)(2\varepsilon + n^2)}{\varepsilon(n^2 + 2)^2}$$

has been used with success with numerous anisotropic substances by Böttcher (" Theory of Electric Polarisation," Elsevier Publ. Co., Amsterdam, 1952, pp. 186—187, 298, 323—328). The results thereby obtained showed a smooth variation of the dipole moments of the phosphonates with the molecular weight, a decline of the moment with increasing molecular weight tending to an apparent limit of about 2·5 D for esters with an alkyl group greater than 16 carbon atoms in length. As pointed out at that time, such a trend could be real or it could be the result of incomplete validity of the above equation.

In the present series of determinations the dielectric data were obtained for several phosphonates which carry short radicals, and dipole moments were then calculated by Onsager's equation. It was seen that the trend, mentioned above, continued for the lower members of the series, and for a group of diethyl esters resulted in continuation of the smooth curve of dipole moment against molecular weight of the phosphonate alkyl radical. It appeared that such data might be employed for estimation of the link moment for the P–O group by graphic vector addition of the remaining moments in the simple molecules. This determination would be of interest since the link-moment data for this group had been previously estimated only for aromatic compounds (Phillips, Hunter, and Sutton, *J.*, 1945, 146). For such a computation it was necessary to formulate the possible atomic configurations of these esters which would involve rotation of groups about the single bonds. Rotation of either the R or the OR groups, among the lower members of this group, can produce the extreme cases of either the " folded " or the " extended " structures. In the former, the third atom of each chain, attached to the phosphorus atom, would approach the singular O–P link in such a way that an attraction might be

postulated between this oxygen and the hydrogen atom that is connected to the third atom of the chain. Such an attraction could lead to hindrance of free rotation of the side chain and could cause the assumption of a bulb-like form of the molecule. A conclusion of this nature was reached by previous workers in the field of parachor measurements with these compounds (Arbuzov and Vinogradova, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1952, 882, 865, 505; 1951, 733; 1947, 459). Such an interpretation of the structure of the phosphonates, also employed for other esters of phosphorus acids, was attractive from the purely chemical point of view. It afforded a simple explanation for the great increase of reactivity in hydrolysis, ester-exchange reactions, and others, in passing from esters that contain ester groups with two or more carbon atoms, to those esters whose side chains, *in toto*, contain one or two atoms only, *i.e.*, side chains which are too short to " reach " the singular oxygen. Compounds of the second class would lack a screening effect, therefore, which is present in compounds of the first group—a screening effect afforded by the CH_2 or CH_3 groups around the highly polar singular oxygen which is expected to be the point of protonic attack in acid-catalysed reactions. Accordingly, graphic vector addition was performed for the various esters that were examined in this group. In each case the " folded " and the " extended " form were taken as the extreme cases of group rotation, employing for the computations the normally expected component values of: C–P moment 0·9 D, P–O (in ester link) moment 1·2 D, O–P–O angle 118°, C–O–P angle 110°, P–O distance (ester link) 1·84 Å, C–O distance 1·51 Å, C–C distance 1·54 Å, and P–O (singular oxygen) distance 1·5 Å (Arbuzov and Shavsha, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1952, 875). The vectorial addition of the moments, the singular P–O link being omitted, gave resultant vector sums which were closely grouped for all esters in either the folded or the extended form: the former gave a range of 2·9—3·4 D, the latter 0·5—1·0 D. However, the " folded " models had the resultant vector directed essentially along the singular P–O link and in the same direction as, but in opposite sense from, the expected polarity of the P–O link. Coupled with the actual calculated values of the total molecular moment (by Onsager's equation), the assumption of the " folded " structure would call for the P–O moment link of some 6·3—6·7 D, a value that is more than twice the expected one. The " extended " structures gave the resultant moments (lacking the P–O link moment) which were directed in the same sense as the expected vector of the singular P–O moment, and the P–O link moments calculated on this basis ranged closely at 2·2—2·8 D for the various esters. This value is somewhat smaller than the value of 3·5 D assumed by Arbuzov and Shavsha (*loc. cit.*). Thus, the results secured through Onsager's equation appear to make it clear that, although the " folded " structure is not completely excluded, yet it is certainly not the predominant form that is assumed by the alkylphosphonates at room temperature.

Although the comparison previously obtained of the molecular dipole moment of diethyl ethylphosphonate as calculated by the Onsager equation and as obtained by extrapolation method from dilute-solution data in *n*-heptane appeared to indicate a satisfactory agreement of the two sets of data (Kosolapoff, *loc. cit.*), yet it was felt that the wide spread of the total molecular moments as estimated by the Onsager equation in this family of compounds might indicate an apparent spread only, and not reflect the true electric dipoles of the molecules. Accordingly, we applied the empirical formula proposed recently by Buckingham and Le Fèvre [*J.*, 1952, 1932; formula (5)] for the estimation of dipole moments from dielectric and dimensional data on pure liquids of anisotropic character, *viz.* (for notation, see *idem, ibid.*):

$$\frac{\mu^2_l}{\mu^2_g} = 1 + \frac{\varepsilon - 1}{\varepsilon + 2}(e^{x^2} - 1) - \frac{1{\cdot}69\, e^{x^2}(\varepsilon - 1)(n^2 + 1)(\varepsilon - n^2)}{\varepsilon^2 n^2 (e^{x^2} + 1)\, e^{M/dABC}}$$

In view of the considerable success with which this formula was applied to a varied group of anisotropic materials, it was felt that the results obtained with it may be a better indication of the true dipole moments of the phosphonates than is afforded by the Onsager formula. The results of this set of calculations showed a much closer grouping of the dipole moments among the esters than was obtained through Onsager's formula, with

general lowering, the extent of which varied with different compounds. In the computations we made use of dimensions of the molecules that would be expected of the " folded " and the " extended " forms. This was necessary because the formula contains an implicit function of molecular shape (or area) which, of course, differs for the two possible extreme forms. The root-mean-square values of these data were then derived, it being deemed reasonable to use them for the representation of the moments of molecules in which rotation of groups leads to constant variation of one form to the other. For the propyl derivative, three positions of the alkyl group were taken into consideration. No attempt was made to apply Buckingham and Le Fèvre's formula to the higher alkylphosphonates, owing to the very great number of possible chain configurations caused by rotation in the long chains.

The values of the dipole moments calculated by the two formulæ are listed in Table 1. In addition, the dipole moment of diethyl *p*-tolylphosphonate is included for an example of the effect produced by the interposition of the phenyl group between the ester and the methyl radicals; only the Onsager formula was used for this computation.

TABLE 1. *Dipole moments of dialkyl alkylphosphonates.*

		μ, in D.			
		From Onsager's formula	From Buckingham and Le Fèvre's formula		
No.	Ester		" Folded "	" Extended "	R.M.S.
1	$MeP(O)(OMe)_2$	3·62	3·04	2·48	2·78
2	$EtP(O)(OMe)_2$	3·38	2·51	2·42	2·47
3	$MeP(O)(OEt)_2$	3·33	2·82	3·39	3·11
4	$EtP(O)(OEt)_2$	2·95	2·46	2·64	2·55
5	$PrP(O)(OEt)_2$	2·94	2·58	2·86, 3·39	2·96
6	$Pr^iP(O)(OEt)_2$	2·85	2·50	2·98	2·75
7	$MeP(O)(OPr^i)_2$	2·83	2·70	2·86	2·78
8	p-MeC_6H_4·$P(O)(OEt)_2$	3·53	—	—	—

Since the calculation of the root-mean-square values listed in Table 1 implies the constant variation of the shape and dimensions of the molecules, no attempt at estimation of the P–O link moments from these values was made, since such computation necessitates assumptions as to definite vector directions of the components.

EXPERIMENTAL

Preparation of Compounds.—The methylphosphonates were prepared by the Arbuzov reaction of methyl iodide with tri*iso*propyl phosphite, which yielded 90% of very pure di*iso*propyl methylphosphonate. This method avoids the possible contamination of the methylphosphonate which would be expected in a reaction of methyl halide with a trialkyl phosphite containing primary alkyl radicals, other than methyl. The resulting ester was hydrolysed by refluxing overnight with concentrated hydrochloric acid. The solution was dehydrated by azeotropic distillation with benzene–toluene, after which the mixture was cooled, yielding a nicely crystalline layer of methylphosphonic acid, which was rinsed with dry benzene and treated with a slight excess of phosphorus pentachloride. Distillation gave an 85% yield of methylphosphonyl dichloride, b. p. 163°/756 mm., which was dissolved in dry benzene, and the solution was slowly added with stirring to a solution of slightly more than 2 equivs. of metallic sodium in either methanol or ethanol (dry). The slight excess of the alkoxide ensured the isolation of halogen-free esters, which were obtained in 78—84% yields.

Ethylphosphonates were obtained similarly from diethyl ethylphosphonate, which in turn was prepared conventionally from ethyl iodide and triethyl phosphite. Ethylphosphonyl dichloride, used as the intermediate, was obtained in 89% yield and boiled at 179°/756 mm.

Propyl- and the *iso*propyl-phosphonates were prepared (75—84% yield) by reaction of the corresponding bromides with diethyl sodiophosphonate in dry benzene solution by conventional procedure.

Diethyl *p*-tolylphosphonate was prepared by treatment of the pure *p*-tolylphosphonic acid (m. p. 195°) with phosphorus pentachloride, followed by conventional esterification of the resulting dichloride with absolute ethanol under slightly reduced pressure.

All the esters were carefully distilled through an efficient ring-packed column and only the middle cuts were employed for the determination of the physical constants, although the entire specimens showed a constant b. p.

Determination of Dipole Moments.—The values of the physical constants, determined at 30°, are shown in Table 2. The measurements of the dielectric constants were made as described previously (Kosolapoff, *loc. cit.*).

TABLE 2. *Physical constants of the phosphonates.*

Ester *	B. p./mm.	n_D^{30}	d_4^{30}	ε^{30}	$[R_D]$, found	$[R_D]$, calc.†
1	79·5°/20	1·4099	1·1507	20·68	26·69	26·92
2	82°/18	1·4128	1·1029	15·89	31·19	31·54
3	85°/15	1·4101	1·0406	13·405	36·20	36·16
4	86°/14	1·4108 ‡	1·0158 ‡	10·653 ‡	40·56	40·77 §
5	104°/17	1·4169	0·9937	9·452	45·54	45·39
6	94°/17	1·4130	0·9914	8·481	45·27	45·39
7	89°/18	1·4062	0·9734	8·061	45·44	45·39
8	100°/0·4	1·4931	1·0834	11·18	61·17	60·26 †

* See Table 1.

† The atomic refraction of phosphorus for the phosphonates was taken at the accepted value of 4·27; this has been established only for the aliphatic compounds thus far. It appears that a higher value is in order for the aromatic members.

‡ At 32°. § Reported earlier (*loc. cit.*).

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Hydrolytic Decomposition of Esters of Nitric Acid. Part III. Kinetic Evidence for Ion Exchange between Anionic Reagents and the Solvent in the Carbonyl Elimination Reaction ($E_{CO}2$).*

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The effect of attack by ethoxide ion, resulting from the equilibrium $Y^- + EtOH \rightleftharpoons HY + OEt^-$ (I), on the determined velocity coefficients $kE_{CO}2$ for the strictly bimolecular elimination reaction $Y^- + CH_2Ph{\cdot}O{\cdot}NO_2 \longrightarrow HY + Ph{\cdot}CH{:}O + NO_2^-$ in 100% ethyl alcohol has been studied when $Y^- = p$-$MeO{\cdot}C_6H_4{\cdot}O^-$, PhO^-, and m- and p-$NO_2{\cdot}C_6H_4{\cdot}O^-$. In the initial absence of the free conjugate acid HY the value of $kE_{CO}2$ drifts markedly downwards during the reaction because much of the elimination is initially due to the much stronger nucleophilic ethoxide ion, the concentration of which is continuously reduced by a mass-law effect on the equilibrium (I) by HY produced as the reaction proceeds. Initial addition of increasing concentrations of free HY eliminates this drift and gradually reduces the value of $kE_{CO}2$ asymptotically to the true value of this constant for attack by Y^-, which is thus determined. The erroneous values which result from neglect of proton transfer from the solvent to an attacking nucleophilic reagent are illustrated, and values of the equilibrium constants K_b' for the four phenols studied are calculated. A plot of the true log $kE_{CO}2$ values against either pK_b' values or pK_a for the phenols in 95% alcohol gives straight lines upon which the value of EtO^- also fits.

A similar, but less marked effect on the concomitant S_N2 reaction $Y^- + CH_2Ph{\cdot}O{\cdot}NO_2 \longrightarrow CH_2Ph{\cdot}Y + NO_3^-$ is also discussed.

ONE method for the diagnosis of mechanism in nucleophilic substitutions and their concomitant elimination reactions is to study the effect of changing the nucleophilic power of the attacking reagent on the course and velocity of the reaction (Gleave, Hughes, and Ingold, *J.*, 1935, 236; Ingold, "Structure and Mechanism in Organic Chemistry," Geo.

* Part II, *J.*, 1952, 1208.

Bell and Sons, London, 1953, pp. 335 *et seq.*). Such nucleophilic reactions have often been studied in proton-donating solvents in which (cf. Bunnett and Zahler, *Chem. Reviews*, 1951, **49**, 399) complications may arise owing to proton transfer from the solvent (often alcohol) to the nucleophilic reagent Y^- and the establishment of the equilibrium

$$Y^- + EtOH \rightleftharpoons HY + OEt^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (I)$$

Such complications were recognised and qualitatively detected by, *e.g.*, Cox (*J.*, 1918, 666; 1922, 493) in his study of the relative reactivities of various alkyl halides with sodium 1- and 2-naphthoxides in alcohol, and by Haywood (*J.*, 1922, **121**, 1904) in similar studies with sodium benzyloxide. There is, however, little or no quantitative information on the magnitude and importance of this effect. Unless the equilibrium (I) were displaced very largely towards the left, the resulting partial replacement of a relatively weak nucleophilic reagent Y^- by the strongly nucleophilic ethoxide ion would cause large increases in the velocity of reaction and thus give quite erroneous values for the velocity coefficients for attack by Y^-.

Clear-cut, quantitative assessment of the magnitude of such ion-exchange with the solvent in kinetic studies might be possible if the following conditions are satisfied. First, the bimolecular reaction studied must be of mechanistic purity throughout the whole range of experiments. Secondly, since it is known that variation in nucleophilic power of different reagents towards hydrogen is usually greater than that towards carbon, a 1 : 2-elimination reaction should demonstrate the effect more markedly than a substitution reaction. Moreover, it would seem (cf. p. 3230) that the lyate-ion effect (Benfey, Hughes, and Ingold, *J.*, 1952, 2488) is much more important in a substitution action, thus giving an abnormally low velocity coefficient for ethoxide ion in ethyl alcohol solution. Finally, the anion Y^- should be a weak base relative to ethoxide ion (if alcohol is the proton-donating solvent), but not so weak that the equilibrium (I) would be displaced almost completely to the left, causing practical exclusion of ethoxide ion from the beginning of the reaction.

In a study (to be fully reported later) the attack of various nucleophilic reagents on benzyl nitrate in 100% ethyl alcohol solution to determine the effect of changes in the reagent on the velocities and relative importance of the two simultaneous reactions :

$$(a)\ Y^- + CH_2Ph{\cdot}O{\cdot}NO_2 \longrightarrow CH_2PhY + NO_3^- \qquad (S_N2)$$

$$(b)\ Y^- + CH_2Ph{\cdot}O{\cdot}NO_2 \longrightarrow Ph{\cdot}CH{:}O + NO_2^- + HY\ (E_{CO}2)$$

(cf. Baker and Easty, *Nature*, 1950, **166**, 156; *J.*, 1952, 1193, 1208), we realised that the attack of various aryloxide ions in the kinetically isolated reaction (*b*) fulfilled the desired conditions. The attack of the phenolic ions (which have the appropriate basic strengths) is at the α-hydrogen atom, and the most significant feature of the carbonyl-elimination reaction (not shared by an olefin elimination) is that it must always be bimolecular, since a rate-determining ionisation $CH_2Ph{\cdot}O{\cdot}NO_2 \rightleftharpoons CH_2Ph{\cdot}\overset{+}{O} + NO_2^-$ is extremely improbable, especially in dry alcohol as solvent. Moreover this conclusion would be unaffected by any intrusion of a unimolecular mechanism in the substitution reaction (*a*) because we have found that this reaction with benzyl nitrate, as with the corresponding halides, is on the borderline S_N2—S_N1 mechanism. Early results (cf. Baker and Neale, *Nature*, 1953, **172**, 583) strongly suggested the incursion of ethoxide ion in these reactions. Thus the velocity coefficients of both the S_N2 and $E_{CO}2$ reactions for attack by equimolecular solutions of either sodium hydroxide (OH^-) or sodium (OEt^-) dissolved in 100% ethyl alcohol were almost identical. This indicated that the attack was essentially by ethoxide ions in both cases and hence that, when $Y^- = OH^-$, the equilibrium (I) is displaced very largely to the right in the presence of small concentrations of water. This conclusion was independently confirmed by Caldin and Long (*ibid.*, p. 583; cf. Williams and Bost, *J. Chem. Phys.*, 1936, **4**, 251).

If, owing to equilibrium (I), aryloxide ions give rise to an appreciable initial concentration of ethoxide ions, there will be two carbonyl-elimination reactions (*b*) proceeding simultaneously, one with aryloxide and the other with ethoxide ion as the nucleophilic

reagent. Because of its much greater nucleophilic power, that with ethoxide ion will have much the greater velocity, notwithstanding the low concentration of ethoxide ions. As the reaction with the aryloxide ion proceeds, increasing concentrations of the conjugate acid ArOH are produced and will, by displacement of the equilibrium (I) to the left, continually decrease the concentration of ethoxide ion, which is inversely proportional to the concentration of ArOH. This would lead, as is observed, to a marked downward drift in the experimental value of $kE_{CO}2$ as the reaction proceeds. Bearing in mind the simultaneous occurrence of two substitution reactions (*a*) (with aryloxide and ethoxide ions) and a superimposed solvolysis (for which correction can be made), the task of separately evaluating the velocity coefficients of each of the four simultaneous reactions is rather formidable, requiring determination of at least four entities (*e.g.*, the concentrations of NO_3^-, NO_2^-, ArOH, and $Ph{\cdot}CH_2{\cdot}OAr$) as functions of time. A simpler experimental approach to the problem seemed to be the initial addition of increasing concentrations of the free conjugate acid ArOH, first, to swamp the small concentration changes consequent on the production of a phenol by reaction (*b*) and, secondly, by a mass law effect on the equilibrium

TABLE 1. *Values of* kS_N2 *and* $kE_{CO}2$ *(both corrected) for the reaction between* Y^- *and* $PhCH_2{\cdot}O{\cdot}NO_2$ *in dry ethyl alcohol at 60·2° in the presence of varying concentrations of free* HY.

Expt.	Y⁻	Excess of HY, (mole l.⁻¹)	Initial concn. (mole l.⁻¹) [$CH_2Ph{\cdot}ONO_2$]	[Y⁻]	10^5k_2 (l. mole⁻¹ sec.⁻¹) S_N2	$E_{CO}2$
1	EtO^-	—	0·0400	0·1026	100 ± 10	1345 ± 10
2	p-$MeO{\cdot}C_6H_4O^-$	0·0019	0·0500	0·0970	122 ± 5	99·2 → 74·5
3	,,	0·0382	0·0529	0·1021	116 ± 2	34·1 → 32·0
4	,,	0·0622	0·0516	0·1000	114 ± 2	23·5 ± 0·3
5	,,	0·0967	0·0529	0·1024	112 ± 2	17·3 ± 0·1
6	,,	0·2025	0·0530	0·0990	103 ± 0·5	11·1 ± 0·05
[7	,,	0·5015	0·0597	0·1097	83·2 ± 0·6	6·38 ± 0·02]
8	$C_6H_5{\cdot}O^-$	0·006	0·0480	0·0927	74 ± 2	48·8 → 36·8
9	,,	0·0252	0·0505	0·0935	68·7 ± 1	26·7 → 22·6
* 10	,,	0·0333	0·0536	*0·0286*	(74·8 ± 1)	21·6 → 20·2
* 11	,,	0·0674	0·0896	*0·2095*	(63·4 ± 1)	12·8 ± 0·1
12	,,	0·0701	0·0510	0·0993	66·3 ± 1	12·7 ± 0·1
* 13	,,	0·1010	0·0530	*0·0400*	(70·2 ± 1)	9·9 ± 0·1
14	,,	0·1080	0·0477	0·0915	64·3 ± 1	9·7 ± 0·1
15	,,	0·2275	0·0514	0·1000	59·1 ± 1	6·30 ± 0·1
16	,,	0·3087	0·0478	0·0897	59·1 ± 1	5·28 ± 0·1
[* 17	,,	0·7244	0·0541	*0·0468*	(48·1 ± 1)	2·97 ± 0·03]
[18	,,	0·9202	0·0502	0·0888	43·6 ± 1	2·44 ± 0·02]
19	m-$NO_2{\cdot}C_6H_4{\cdot}O^-$	0·001	0·0545	0·0898	25·4 ± 1	2·35 → 1·55
20	,,	0·1589	0·0519	0·0988	20·5 ± 0·2	0·584 ± 0·007
21	,,	0·2572	0·0528	0·1004	18·1 ± 0·2	0·440 ± 0·005
22	,,	0·4138	0·0565	0·1019	16·1 ± 0·2	0·360 ± 0·004
[23	,,	0·9986	0·0543	0·1013	10·5 ± 0·2	0·143 ± 0·003]
24	p-$NO_2{\cdot}C_6H_4{\cdot}O^-$	—	0·0564	0·0983	7·2 ± 0·10	0·20 → 0·15
25	,,	0·0628	0·0514	0·1064	6·07 ± 0·10	0·122 ± 0·01
26	,,	0·0963	0·0489	0·1034	5·51 ± 0·07	0·108 ± 0·01
27	,,	0·1882	0·0537	0·1108	5·38 ± 0·03	0·100 ± 0·01
[28	,,	0·3937	0·0508	0·1081	4·39 ± 0·10	0·076 ± 0·01]
† 29	$C_6H_5O^-$	0·0297	0·0541	0·1039	14·9 ± 0·1	3·75 → 3·38
† 30	,,	0·0464	0·0513	0·1036	14·9 ± 0·1	2·72 ± 0·06
† 31	,,	0·0908	0·0531	0·1032	14·4 ± 0·1	1·77 ± 0·03
† 32	,,	0·2121	0·0555	0·1373	13·3 ± 0·1	1·08 ± 0·01

* Determined at a different [NaOPh] which (p. 3230) causes some change in kS_N2 (values in parentheses). † At 45°.

(I), ultimately to effect the more or less complete suppression of ethoxide ion from the beginning of the experiment. If these aims could be achieved before the concentration of the phenol is large enough to alter seriously the nature of the medium, such additions of the free phenol in increasing amounts should gradually eliminate the drift in the value of $kE_{CO}2$ throughout any one run and cause successive decreases in $kE_{CO}2$ towards an asymptotic value which is the true value of this coefficient for attack by the reagent OAr^-. Both these expectations have been completely realised in the carbonyl-elimination reaction for

attack by four different aryloxide ions on benzyl nitrate in 100% ethyl alcohol as solvent, *viz.*, $OAr^- = p\text{-}MeO\cdot C_6H_4\cdot O^-$, OPh^-, *m*- and *p*-$NO_2\cdot C_6H_4\cdot O^-$, and, in the case of phenoxide, at two temperatures. The effects of addition of increasing amounts of the corresponding free phenol on the separate values of kS_N2 and $kE_{CO}2$ (corrected for the solvolysis of benzyl nitrate in 100% alcohol, which gives no elimination) are in Table 1. When a drifting velocity coefficient was obtained the limits of the (regular) drift from the initial to the final readings are indicated; where no such significant drift occurred, the mean deviation from the mean is shown. It was shown that the presence of 0·994M-phenol caused only a ~7% rise in the velocity of the solvolysis of benzyl nitrate in dry ethyl alcohol ($10^5k_1^{60\cdot2°}$ increased from 0·119 to 0·127 sec.$^{-1}$) which makes no significant difference to the small correction for solvolysis. The observation that, at constant concentration of phenol, the experimental value of $kE_{CO}2$ is independent of the initial aryloxide ion concentration, shows that the elimination by this ion is a true second-order reaction.

Before a quantitative analysis of the results is given attention may be directed to a few general features. In agreement with the postulated effect of the free phenol on the equilibrium (I) it is found that, as the basic strength of the aryloxide ion decreases

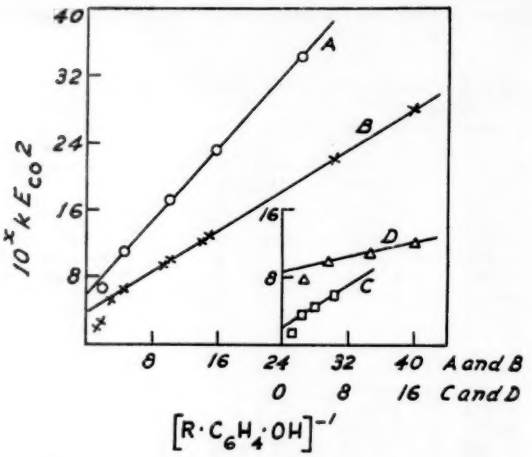

FIG. 1. *Variation of* $kE_{CO}2$ *in the reaction of* $PhCH_2\cdot NO_3$ *with* $R\cdot C_6H_4O^-$ *in the presence of varying* $[R\cdot C_6H_4\cdot OH]$ *in* 100% EtOH *at* 60·2°.

A, R = *p*-MeO; $x = 5$.
B, R = H; $x = 5$.
C, R = *m*-NO_2; $x = 6$.
D, R = *p*-NO_2; $x = 7$.

($p\text{-}MeO\cdot C_6H_4\cdot O^- > OPh^- > m\text{-} > p\text{-}NO_2\cdot C_6H_4\cdot O^-$) the observed drift in $kE_{CO}2$ in the absence of excess of phenol becomes less marked (Table 1, Expts. 2, 8, 19, 24) and this initial value is closer to the value observed in the presence of a moderate excess of phenol, *i.e.*, as the acid strength of the phenol increases, the initial equilibrium (I) lies further to the left so that much smaller concentrations of ethoxide ion are initially present. As expected, gradual replacement of ethoxide ion by aryloxide ion has a much smaller effect on kS_N2 than on $kE_{CO}2$. The results of Quayle and Royals (*J. Amer. Chem. Soc.*, 1942, **64**, 227) for the action of 0·05M-sodium phenoxide in dry ethyl alcohol on *n*-butyl bromide provide a further illustration of the relatively small effect on a substitution reaction. Extrapolation of their data gives $10^5k_2^{55°} = 26\cdot8$ l. mole^{-1} sec.$^{-1}$. For the similar attack by sodium ethoxide the value is $10^5k_2^{55°} = 43\cdot9$ l. mole^{-1} sec.$^{-1}$ (Dhar, Hughes, Ingold, and Masterman, *J.*, 1948, 2055). From our calculation (p. 3230) of the equilibrium constant between phenoxide ion and ethyl alcohol (at 60°), the initial concentration of ethoxide ion in Quayle and Royals's experiment would be ~0·005M, whence the true value of $10^5k_2^{55°}$ for phenoxide can be calculated to be 24·9 l. mole^{-1} sec.$^{-1}$, representing only about a 7% error in their recorded value.

When the concentration of added phenol becomes very large (Table 1, Expts. 7, 17, 18, 23, 28) effects due to the medium and other disturbing factors enter. In Expt. 18, for example, the solvent contains ~6 moles % (~10% by weight) of phenol and abnormally large falls in both kS_N2 and $kE_{CO}2$ are observed. When such experiments are omitted,

a plot of $kE_{CO}2$ against the reciprocal of the phenol concentration gives a good straight line (Fig. 1), extrapolation of which to $[ArOH]^{-1} = 0$ should give the *true* value of $kE_{CO}2$ for the particular aryloxide ion. The values so obtained at 60·2° are :

$ArO^- =$	*p*-MeO·C_6H_4·O^-	OPh^-	*m*-NO_2·C_6H_4·O^-	*p*-NO_2·C_6H_4·O^-
True $10^5kE_{CO}2$ (l. mole^{-1} sec.$^{-1}$)	5·63	3·80	0·22	0·085
,, 10^5kS_N2 (l. mole^{-1} sec.$^{-1}$)	110	60	13·7	5·0

$10^5kE_{CO}2$ for phenoxide at 45° = 0·7 l. mole^{-1} sec.$^{-1}$.

The large error introduced by neglecting proton-exchange between the solvent and an attacking nucleophilic anion of moderate basic strength is thus clearly demonstrated. For phenoxide in the reaction studied the uncorrected value of $kE_{CO}2$ is ~13 times the true value, which suggests that it is necessary to re-examine results previously obtained in which this factor has been ignored. We have not yet examined how important is the equilibrium $NR_3 + EtOH \rightleftharpoons N^+HR_3 + OEt^-$ in the case of attack by neutral bases, but Betts and Hanmett's results (*J. Amer. Chem. Soc.*, 1937, **59**, 1568) show that it is significant in the case of ammonia.

Analysis of our data gives further interesting information. By using the value $k^{OEt^-}E_{CO}2 = 1345 \times 10^{-5}$ (Table 1, No. 1) and the true value of $k^{OPh^-}E_{CO}2 = 3{\cdot}8 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$, it is possible to calculate, in any one experiment, the concentrations of phenoxide and ethoxide ions present at each stage of the reaction. The equation representing total carbonyl elimination, determined by the amount of nitrite ion produced at time *t*, is :

$$d[NO^-_2]/dt = k^{OPh^-}E_{CO}2.[Ph{\cdot}CH_2{\cdot}O{\cdot}NO_2][OPh^-] + k^{OEt^-}E_{CO}2.[Ph{\cdot}CH_2{\cdot}O{\cdot}NO_2][OEt^-] \quad (II)$$

If the initial concentration of benzyl nitrate = *a*, the total alkali concentration = *b*, and, at time *t*, the amount of total second-order reaction (substitution + elimination) = *x*, and the instantaneous values of the concentrations of phenoxide and ethoxide ions are, respectively, *p* and *e*, then

$$p + e = (b - x)$$

and $$d[NO_2^-]/dt = k^{OPh^-}E_{CO}2\,.\,(a - x)(p) + k^{OEt}\,E_{CO}2\,.\,(a - x)(e)$$

whence $d[NO_2^-]/dt(a - x) = (\text{say})\ M = k^{OPh^-}E_{CO}2\,.\,p + k^{OEt}\,E_{CO}2\,.\,(b - x - p)$

therefore, $$p = [M - k^{OEt^-}E_{CO}2\,.\,(b - x)]/[k^{OPh^-}E_{CO}2 - k^{OEt^-}E_{CO}2]$$

The value of $d[NO_2^-]/dt$ can be obtained from the tangent at time *t* to the curve obtained by plotting $[NO_2^-]$ against *t*, whence *M* and thus *p* and *e* can be determined. Application of this method to Expt. 8 (no appreciable excess of phenol initially present) shows that, at the beginning of the run, the ratio $\{[OPh^-]\}/\{[OPh^-] + [OEt^-]\} = 0{\cdot}97$, *i.e.*, about 3% of the total alkali present is ethoxide ion. This amount gradually decreases throughout the run until, towards the end, it has been reduced to ~2%. Because of the much larger value of $k^{OEt^-}E_{CO}2$ this means that ~85% of the total carbonyl elimination is due to ethoxide ion and only 15% to phenoxide. Even in Expt. 16, approximately 10% of the carbonyl elimination is still due to ethoxide.

The results also permit an assessment to be made of the values of the equilibrium constant $K_b' = [ArOH][OEt^-]/[OAr^-][EtOH]$ for each of the phenols. The relation (II) can be rewritten as

$$d[NO_2^-]/dt = k^{OAr^-}E_{CO}2\,.\,[Ph{\cdot}CH_2{\cdot}O{\cdot}NO_2][OAr^-] + k^{OEt^-}E_{CO}2\,.\,[Ph{\cdot}CH_2{\cdot}O{\cdot}NO_2][OAr^-]K_b'[EtOH]/[ArOH]$$

whence $$d[NO_2]/dt[Ph{\cdot}CH_2{\cdot}O{\cdot}NO_2][OAr^-] = k^{OAr^-}E_{CO}2 + k^{OEt^-}E_{CO}2\,.\,K_b'[EtOH]/[ArOH] = kE_{CO}2 \text{ experimental} \quad (III)$$

since, in the presence of excess of ArOH, the ethoxide ion concentration is small and no serious error is introduced if the measured alkali concentration is substituted for [OAr^-]. Thus the slope of the straight line obtained by plotting $kE_{CO}2$ (experimental) against $[ArOH]^{-1}$ (p. 3228) gives $k^{OEt^-}E_{CO}2 \cdot K_b'[\Sigma EtOH]$ whence K_b' (in terms of concentration, not of activities) is obtained, the concentration of ethyl alcohol at 60° being taken as 16·4M. The values (at 60·2°) thus obtained are:

ArOH =	*p*-MeO·C_6H_4·OH	PhOH	*m*-NO_2·C_6H_4·OH	*p*-NO_2·C_6H_4·OH
$10^7K_b'$	493	276	26	0·9

It must be remembered that all the errors, both in the isolation of $kE_{CO}2$ from the total second-order coefficient, and in the extrapolation of $kE_{CO}2$ to $[ArOH]^{-1} = 0$, cumulatively affect this determination of K_b', yet a Brönsted plot of log $kE_{CO}2$ against pK_b' approximates closely to a straight line (Fig. 2) upon which ethoxide also falls into place. If instead of

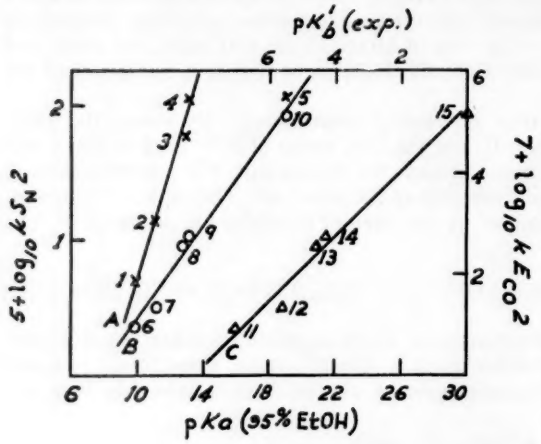

FIG. 2. *Brönsted plots of* kS_N2 *and* $kE_{CO}2$ *for the reaction of* $PhCH_2 \cdot NO_3$ *with* RO′ *in* 100% EtOH *at* 60·2°.

Curves: $A = kS_N2$. B and C, $kE_{CO}2$.

Experimental points:
1, 6, 11. *p*-NO_2·C_6H_4·O^-.
2, 7, 12. *m*-NO_2·C_6H_4·O^-.
3, 8, 13. PhO^-.
4, 9, 14. *p*-MeO·C_6H_4·O^-.
5, 10, 15. EtO^-.

our pK_b', the recorded values of pK_a for the phenol in 95% aqueous alcohol (Schwarzenbach and Rudin, *Helv. Chim. Acta*, 1939, **22**, 360) (or in water) are used a better straight-line plot results.

Theoretically, similar analyses could be applied to the data for kS_N2, but reasons have already been given why less clear-cut results might be expected in the substitution reaction. In practice we have found evidence of other disturbing factors. The decrease in kS_N2 caused by increasing concentrations of the free phenol is expressed by an equation $kS_N2 =$ constant $+ A/[ArOH]$, of the same type as (III), and the values of kS_N2 obtained by extrapolation to $[ArOH]^{-1} = 0$ are given above (p. 3228). The observed decrease is, however, larger than would be expected if $A = k^{OEt^-}S_N2 \cdot K_b'$, when the previously-determined values of K_b', from the elimination reaction, are used. Compared with that for phenoxide, the value of kS_N2 for ethoxide is abnormally low. This may be accounted for, at least partly, by the lyate-ion effect discussed by Benfey, Hughes, and Ingold (*loc. cit.*). The absence of such an effect in the elimination is understandable since it is only another hydrogen nucleus and not carbon which is attacked. Other abnormalities cannot be so explained. Unlike the constancy observed for $kE_{CO}2$, the value of kS_N2 at constant phenol concentration decreases slightly with increasing concentration of sodium aryloxide, *e.g.*, with sodium phenoxide in 100% ethyl alcohol and a 0·07M-excess of phenol:

[NaOPh] (M)	0·04	0·1	0·2
10^5kS_N2 (l. mole.$^{-1}$ sec.$^{-1}$)	70·8	66·3	63·4

Another anomally was observed in the effect of increasing the ionising power of the solvent by addition of water to the alcohol. Whereas increase in the water content of the solvent causes a small *decrease* in the values of both kS_N2 and $kE_{CO}2$ for attack by hydroxide ion,

in agreement with the Hughes–Ingold theory (*J.*, 1935, 244) for a reaction which involves distribution of a fixed charge in the transition state, the corresponding value of kS_N2 for phenoxide ion attack is considerably *increased*, in direct opposition to the requirements of this theory:

Solvent: % of H_2O in EtOH	0	40	55
$10^4k^{OH}S_N2$ (l. mole.$^{-1}$ sec.$^{-1}$)	10	—	5·5
$10^3k^{OH}E_{CO}2$ (l. mole.$^{-1}$ sec.$^{-1}$)	13·45	1·98	0·9
$10^4k^{OPh^-}S_N2$ (l. mole.$^{-1}$ sec.$^{-1}$)	7·8	16·0	22·4

The only tentative explanation we can suggest * for these anomalies is that there is some degree of ion association in the sodium aryloxide, a view which has been suggested by various workers (Hardwick, *J.*, 1935, 141; Mitchell, *J.*, 1937, 1792; Woolf, *ibid.*, p. 1172; cf. also Bell, "Advances in Catalysis," Academic Press, New York, 1952, Vol. 4, 154). It must be assumed that whilst the undissociated sodium aryloxide or the ion-pair $ArO^-\}Na^+$ is as effective as the aryloxide ion for attack on the small exposed hydrogen nucleus (elimination reaction), they are not so effective for attack on the more effectively screened carbon nucleus (substitution reaction). Any such ion association would be expected to increase both with increasing concentration of sodium aryloxide in 100% alcohol (and thus account for the observed drop in kS_N2 with 0·2M-sodium aryloxide) and with decrease in the ionising power of the solvent (thus explaining the much smaller value of $k^{OPh^-}S_N2$ in 100% alcohol). It is, of course, recognised that addition of water to the solvent introduces the new equilibria $HOH + OEt^- \rightleftharpoons EtOH + OH^-$ and $HOH + PhO^- \rightleftharpoons PhOH + OH^-$, both interrelated with equilibrium (I) (which has been the main concern in this communication), thus introducing further complications. It is the data for the carbonyl-elimination reaction which most clearly demonstrate the importance and magnitude of the hitherto largely neglected effect of proton-transfer from the solvent to an attacking nucleophilic ion in kinetic studies.

Experimental

Solvents and Materials.—Dry 100% ethyl alcohol was prepared either by Smith's (*J.*, 1927, 1288; cf. Manske, *J. Amer. Chem. Soc.*, 1931, **53**, 1106) or by Lund and Bjerrum's method (*Ber.*, 1931, **64**, 210), with rigid precautions to exclude atmospheric moisture and carbon dioxide. It was stored under dry nitrogen in the dark, and had d^4_{20} 0·7893 (in agreement with that for 100% ethyl alcohol given in International Critical Tables). The maximum water content, determined by Smith's method (*J.*, 1927, 1284), was 0·04%; the alcohol was free from carbonyl compounds (2 : 4-dinitrophenylhydrazine) and was stable to alkali over long periods at 60°. The rate of solvolyses of benzyl nitrate ($10^6k_1^{60} = 1·19$ sec.$^{-1}$) with this solvent remained unchanged after it had been stored for 10 months. Addition of 1% of water to the 100% alcohol decreased the value of $10^2k_2^{60}$ for the alkaline hydrolysis of benzyl nitrate from 1·47 to 1·37 l. mole^{-1} sec.$^{-1}$.

Aqueous-alcohol solvents were prepared by mixing x volumes of this dry alcohol with $(100 - x)$ volumes of water to give "x vol. %" alcohol.

Benzyl Nitrate.—Dry benzyl chloride, b. p. 74·5°/15 mm. (50 g.), in dry ether (50 ml.) was kept with *very* finely powdered silver nitrate (75 g.) at room temperature for 12 hr., and was then refluxed at 70—75° (with exclusion of moisture and carbon dioxide) until free from chloride. Ether was distilled from the dried (calcium nitrate) filtrate from silver residues, and the residue was repeatedly fractionated through a column from powdered silver nitrate and calcium carbonate to give a specimen, b. p. 59·0°/0·4 mm., n^{20}_D 1·5206 (Found: C, 55·2; H, 4·2. Calc. for $C_7H_7O_3N$: C, 54·9; H, 4·6%. Purity by complete hydrolysis, 100%). It was best stored in a brown stoppered bottle in a calcium nitrate desiccator and was repurified whenever any deviation from 100% purity by complete hydrolysis was detected.

p-Methoxyphenol was purified by repeated crystallisation from benzene–ligroin (b. p. 60—80°) at −15° in the absence of oxygen, to give colourless crystals, m. p. 56°. With sodium ethoxide solution prepared from dry alcohol (saturated with nitrogen) and clean sodium, colourless solutions (free from oxidation products) of the sodium salt were obtained.

* On the basis of other work (Caldin and Long, in the press) Dr. E. F. Caldin privately suggested that the negative charge distribution in the attacking phenoxide might be *greater* than it is in the transition state, where it is more concentrated on the separating nitrate anion, thus leading to *greater localisation* of the charge in the transition state.

m-Nitrophenol was crystallised from benzene and chloroform to constant m. p. 97·5—98°. *p*-Nitrophenol was crystallised from dry toluene to give pale yellow crystals, m. p. 114°, which gradually changed to the reddish β-form (Sidgwick, *J.*, 1915, **107**, 676, 1208). Subsequent crystallisation from water gave the colourless α-form, m. p. 114°, stable to light. It was dried over magnesium perchlorate *in vacuo*.

" AnalaR " phenol, dried *in vacuo* ($MgClO_4$), was used without further purification.

Velocity Determinations.—The general techniques were those previously used (Baker and Easty, *loc. cit.*), refined and modified to suit each particular reagent. Since reaction velocities with benzyl nitrate (deliberately chosen to exclude olefin-elimination reactions) are much greater than those with alkyl nitrates, a sealed glass bulb technique could be employed for both alkaline and solvolytic reactions. Spherical bulbs (2 ml.) were blown from " Monax " glass quill tubing with very small free space, although it was proved that neither considerable variation in the " free-space " volume nor addition of powdered glass had any effect on the values of the velocity coefficients. Bulbs were filled at room temperature from an all-glass apparatus incorporating a gravity-filled pipette suitably connected to a capillary delivery tube, and were all plunged into the thermostat at the same time. Initial concentrations, determined by direct weighing and checked by complete hydrolysis values, were corrected for the amount of reaction which had occurred before temperature equilibrium had been attained (by initial sampling at zero time), for solvent expansion, or for the (small) volume of the liquid ester whenever a known volume of the more concentrated alkali solutions was added directly to the weighed ester. All methods used gave velocity coefficients which agreed to within ±1%. Thermostats were constant to at least ±0·05°. Reaction samples were " frozen " by breaking the bulbs under neutral ether at −10° (when aqueous extracts for nitrate and nitrite determinations were required) or cold acetone (when only acid–alkali titrations were used, bromophenol-blue then being the indicator). The most suitable indicator was determined, by preliminary experiments, for each reagent used. In aqueous extracts acidity was determined by titration with 0·01N-potassium hydroxide, and alkalinity with either 0·01 or 0·02N-sulphuric acid, using methyl-red or methylene-blue screened neutral-red (when large concentrations of nitrite were present), with usual expulsion of carbon dioxide at the end point.

Sodium phenoxide and *p*-methoxyphenoxide were best determined by breaking the sample under carbon dioxide-free distilled water (organic matter being precipitated) and direct titration with acid using screened methyl-red. This avoided complications otherwise encountered due to the presence of nitrous acid. With *m*-nitrophenoxide the very small amount of nitrite formed did not interfere, neither did the indicator property of this reagent, and direct titration of the aqueous extract using acid and screened methyl-red was satisfactory. *p*-Nitrophenoxide was determined by delivery of the sample into an excess of a cold, standard alcoholic solution of hydrochloric acid and back-titration with alkali using bromophenol-blue.

Nitrite determinations were carried out on an aliquot portion of the aqueous extract diluted so that nitrite was in the range 2—10 × 10^{-6}M, by a modification of the Griess–Ilosvay method which involves diazotisation of sulphanilamide and coupling with *N*-1-naphthylethylenediamine dihydrochloride (Shinn, *Ind. Eng. Chem. Anal.*, 1941, **13**, 33; Barnes and Folkard, *Analyst*, 1951, **76**, 55). The colour maximum is rapidly attained and stable for several hours and the optical density was determined with a Hilger 760 Spekker Photoelectric Absorptiometer with an Ilford 604 green filter. The calibration curve (from " AnalaR " sodium nitrite) was linear at least up to an optical density of 0·50, and all determinations were effected below this value. The calibration data are:

$10^6[NO_2^-]$ (mole $l.^{-1}$)	2·425	5·050	7·350	10·10	12·60	14·70
Optical density	0·100	0·210	0·350	0·420	0·520	0·615

Even with low concentrations of nitrite the accuracy of this method is 0·5—1% and hence accurate values for $kE_{CO}2$ could be obtained when the elimination was only ~1% of the total reaction.

Nitrate determinations were also made on the aqueous extracts by Baker and Easty's gravimetric method (*loc. cit.*). When nitrite was also present it was first destroyed by a 50% excess of sulphamic acid. The accuracy (±1%) was tested with both " AnalaR " potassium nitrate and aqueous nitric acid:

		Found:	
	Calc.	(*a*) no nitrite	(*b*) +0·02M-nitrite
Potassium nitrate (M)	0·01092	0·01099	0·01087
Nitric acid (M)	0·01037	0·01026	—

Reaction Products.—Proof that nucleophilic substitution occurs solely at carbon was provided by larger-scale experiments under conditions closely similar to those used in kinetic studies. A solution containing 5 g. of benzyl nitrate in dry ethyl alcohol containing 0·0654M-benzyl nitrate, 0·426M-phenol, and 0·131M-sodium ethoxide gave, after refluxing for 48 hr., 4·95 g. of pure (twice crystallised) benzyl phenyl ether, m. p. 38—39° (Found: C, 84·7; H, 6·1. Calc. for $C_{13}H_{12}O$: C, 84·8; H, 6·5%). This corresponds to an isolated yield of 82%, and kinetic experiments show that 10% of benzaldehyde is formed by a concurrent carbonyl elimination reaction.

Calculation of Velocity Coefficients.—In solvolyses the pseudo first-order rate coefficient was calculated from the usual equation using the "long interval" method (Weissberger, "Technique of Organic Chemistry," Vol. VIII, Interscience Publ. Inc., New York, 1953, p. 187). At least ten individual samples were taken in each run, reactions being followed to ~80% completion. In agreement with Winstein (*J. Amer. Chem. Soc.*, 1951, **73**, 2702) rate coefficients, even in mixed solvents, were strictly reproducible to at least 2—3%.

In reactions with anions the experimental second-order coefficient k_2 was determined from the usual equation. Correction for first-order solvolysis was made by using the equation $\bar{k}_2 + t\mathrm{d}\bar{k}_2/\mathrm{d}t = k_2^{\mathrm{corr.}} + k_1/(b - x)$ (Hughes, Ingold, and Shapiro, *J.*, 1936, 225) where $k_2^{\mathrm{corr.}}$ is the true second-order coefficient (substitution + elimination), k_1 = the first-order solvolysis constant, and x is the total reaction at time t. In our experiments $t\mathrm{d}\bar{k}_2/\mathrm{d}t$ was neglible. The percentage of solvolysis (A) is given by

$$A = \frac{100k_1}{k_2^{\mathrm{corr.}}x} \ln\left\{\frac{(k_1/k^{\mathrm{corr.}}) + b}{(k_1/k_2^{\mathrm{corr.}}) + (b - x)}\right\}$$

(Hughes *et al.*, *loc. cit.*). Nitrite determinations permit determination of the percentage of carbonyl elimination (B) whence the percentage of substitution is (100-A-B). Hence the true values of kS_N2 and $kE_{CO}2$ were determined. Application of this method is given in Table 2.

TABLE 2. *Sodium* m-*nitrophenoxide and benzyl nitrate in* 100% EtOH *at* 60°.

Initially, $[NaO{\cdot}C_6H_4(NO_2)] = 0{\cdot}08894$M; $[Ph{\cdot}CH_2{\cdot}O{\cdot}NO_2] = 0{\cdot}05357$M.

$10^4\bar{k}_2$ l. mole^{-1} sec.$^{-1}$	$10^4k_1/(b-x)$ l. mole^{-1} sec.$^{-1}$	$10^4k_2^{\mathrm{corr.}}$ l. mole^{-1} sec.$^{-1}$	Solvolysis (%) calc. (A)	E_{CO} (%) obs. (B)	S_N2 (%) 100-A-B	10^4kS_N2 l. mole^{-1} sec.$^{-1}$	$10^4kE_{CO}2$ l. mole^{-1} sec.$^{-1}$	$10^4\bar{k}E_{CO}2$ [% $E_{CO} \times \bar{k}_2$] l. mole^{-1} sec.$^{-1}$
2·982	0·151	2·831	4·95	—	—	—	—	—
2·972	0·157	2·815	5·03	7·93	87·04	2·580	0·235	0·236
2·885	0·163	2·722	5·13	7·57	87·30	2·505	0·217	0·218
2·890	0·169	2·721	5·22	7·15	87·63	2·516	0·205	0·207
2·882	0·175	2·707	5·29	7·21	87·50	2·501	0·206	0·208
2·970	0·184	2·786	5·41	6·87	87·72	2·583	0·203	0·204
2·936	0·190	2·746	5·49	6·58	87·93	2·554	0·192	0·193
2·852	0·195	2·657	—	—	—	—	—	—
2·915	0·206	2·709	5·69	6·04	88·27	2·535	0·174	0·176
2·925	0·213	2·712	5·77	5·98	88·25	2·539	0·173	0·175
2·923	0·221	2·702	5·87	5·77	88·36	2·536	0·166	0·168
2·932	0·231	2·701	5·97	5·63	88·40	2·539	0·162	0·165
2·975	0·238	2·737	6·05	5·56	88·39	2·575	0·162	0·165
2·912	0·243	2·672	6·10	5·44	88·46	2·517	0·155	0·158

In practice this method is tedious, and the following simpler method was subsequently used. The percentage of the *total* reaction (including solvolysis) proceeding by the elimination route is known from nitrite determinations, whence $\bar{k}E_{CO}2 = \%E_{CO} \times \bar{k}_2$. In practice $\bar{k}E_{CO}2$ was identical with $kE_{CO}2$ calculated by the rigorous method. This is illustrated in the last column of Table 2 and was checked by sample calculations using the rigorous method in other cases. The value of kS_N2 then equals $k_2^{\mathrm{corr.}} - kE_{CO}2$, as above. Not less than ten samples from each run, followed to ~70% completion, were taken; the estimated accuracy of the *separated* rate constants is at least 5%.

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The Chemistry of the Triterpenes and Related Compounds. Part XXVI. The Nature of Polyporenic Acid B.*

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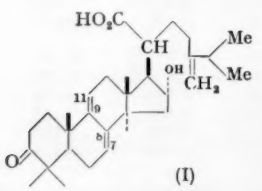
[Reprint Order No. 5362.]

Polyporenic acid B (Cross, Eliot, Heilbron, and Jones, *J.*, 1940, 632) has been shown to be a mixture of 3β : 16α-dihydroxyeburico-8 : 24(28)-dien-21-oic acid and the corresponding dehydro-acid. It is accompanied in *Polyporus betulinus* by the 3β-monoacetates of these acids.

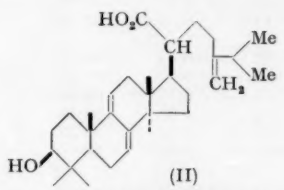
In 1939, Cross, Eliot, Heilbron, and Jones (*J.*, 1940, 632) isolated three acids, polyporenic acids A, B, and C, from the birch-tree fungus, *Polyporus betulinus* Fr. It was suggested that these acids might be triterpenoids and for polyporenic acid B a formula $C_{30}H_{48}O_4$ or $C_{31}H_{50}O_4$ was put forward on the basis of analyses of the acid, m. p. 300—310 (decomp.), and its methyl ester, m. p. 160°. A Zerewitinoff determination on the ester indicated that acid B was a dihydroxy-acid. The work was abandoned in 1940 and it is only recently that it has become possible to examine polyporenic acid B in detail.

Cross *et al.* (*loc. cit.*) indicated that acid B accompanied polyporenic acid C in the ether–acetone extract of fungus which had already been extracted with alcohol to remove polyporenic acid A. With the elucidation of the structure of acid C (I) (Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548; Bowers, Halsall, and Sayer, *J.*, 1954, 3070), and the knowledge that it reacted with Girard's reagent, it was possible to isolate acid B by methylating with ethereal diazomethane the acetone extract of the fungus from which polyporenic acid A had been removed by ethanol extraction, and then subjecting it to a Girard separation. The non-ketonic fraction was chromatographed on alumina and two esters were isolated. One was a methyl dihydroxy-ester ($C_{32}H_{52}O_4$) which formed needles, m. p. 168—171°, from methanol. This is obviously methyl polyporenate B. The other ester was a monoacetoxy-monohydroxy-derivative ($C_{34}H_{54}O_5$) which could be hydrolysed to methyl polyporenate B.

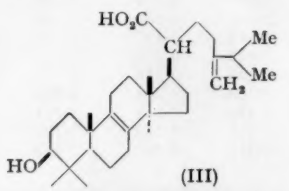
Both esters on spectroscopic examination showed absorption at 2360, 2430, and 2520 Å, corresponding to the presence of 40% (dihydroxy-ester) and 15% (monoacetoxy-monohydroxy-ester), respectively, of the typical 7 : 9(11)-diene chromophore such as is found in polyporenic acid C (I) and dehydroeburicoic acid (II) (Gascoigne, Robertson, and



(I)



(II)



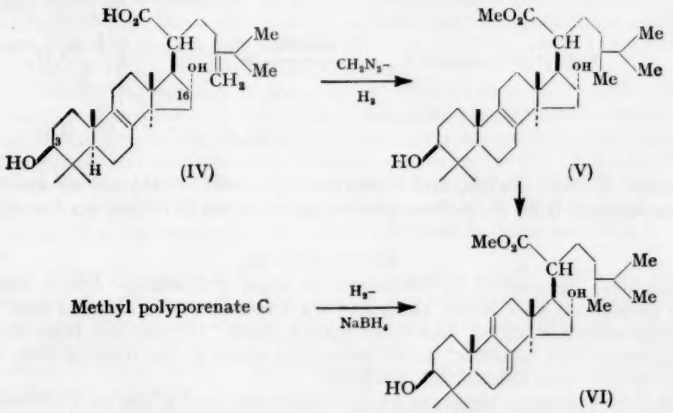
(III)

Simes, *J.*, 1953, 1830). These workers have found that extraction of certain fungi leads to the isolation of practically inseparable mixtures of eburicoic (III) (Holker, Powell, Robertson, Simes, Wright, and Gascoigne, *J.*, 1953, 2422) and dehydroeburicoic (II) acids. It therefore appeared likely that " methyl polyporenate B " was a mixture of the esters of a similar pair of acids. Simple transformations of mixtures of this type do not usually bring about much change in the percentage of dehydro-derivative present [cf. the reactions of a mixture of α-elemolic acid and its dehydro-derivative (Halsall, Meakins, and Swayne, *J.*, 1953, 4139)]. A number of simple reactions with the " methyl polyporenate B " obtained as described above were therefore carried out.

The infra-red spectrum of " methyl polyporenate B " determined in carbon tetrachloride had bands at 3635, 1737, and 1640 and 894 cm.$^{-1}$ indicative of hydroxyl, methoxycarbonyl,

* Part XXV, *J.*, 1954, 3070.

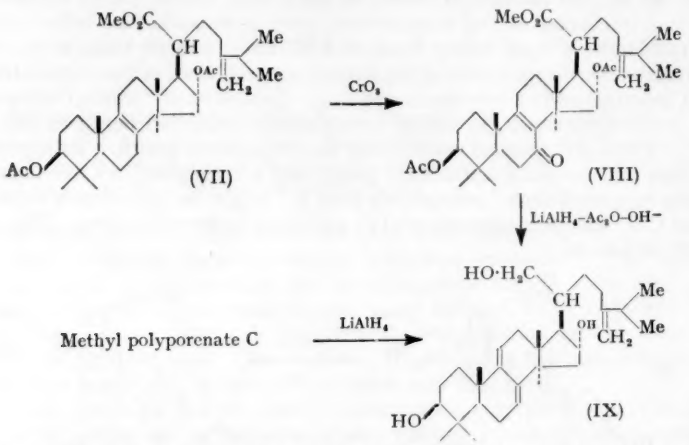
and vinylidene groups, respectively. Acetylation of the ester gave a diacetate which was also obtained by acetylation of the methyl ester monoacetate described above. The light absorptions of the two samples of diacetate were very similar ($\varepsilon_{2430A} = 3930$ and 3740 respectively). Oxidation of the monoacetate gave a mono-ketone, which exhibited, in carbon tetrachloride, a very strong band at 1737 cm.$^{-1}$ but no band at *ca.* 1705 cm.$^{-1}$. This indicates that the oxygen atom of the keto-group and hence of the original free hydroxyl group must be attached to a five-membered ring. Oxidation of " methyl polyporenate B " itself gave a diketone which, in carbon tetrachloride, exhibited bands at 895, 1714, and 1740 cm.$^{-1}$. These are assigned respectively to a vinylidene group, a keto-group in a six-membered ring and the methoxycarbonyl group, and a keto-group in a five-membered ring. These results suggested that " polyporenic acid B " might be very closely related to polyporenic acid C (I) and be a mixture of (IV) and its dehydro-derivative. This was proved to be correct as follows :



" Methyl polyporenate B " was hydrogenated to the dihydro-derivative (cf. V) and this was converted into the corresponding dehydro-compound by oxidation with monoperphthalic acid and treatment of the resulting oxide in boiling ethanol with concentrated hydrochloric acid for two hours. Modifications of this method have been used to convert dihydrolanosteryl acetate (Birchenough and McGhie, *J.*, 1949, 2038), *O*-acetylidhydroeburicoic acid (Lahey and Strasser, *J.*, 1951, 873), and dihydroeuphyl acetate (Barbour, Bennett, and Warren, *J.*, 1951, 2540) into their corresponding dehydro-derivatives. The dehydro-derivative from " methyl dihydropolyporenate B " was identical with methyl 3β : 16α-dihydroxyeburico-7 : 9(11)-dien-21-oate (VI) obtained from methyl polyporenate C by hydrogenation and reduction of the 3-oxo-group with sodium borohydride (Bowers, Halsall, Jones, and Lemin, *loc. cit.*). This interconversion proves the structure of the main component of " polyporenic acid B " apart from the position of the vinylidene group. To locate this group the diacetate of " methyl polyporenate B " (cf. VII) was oxidised to the 7-oxo-derivative (cf. VIII). This was reduced with lithium aluminium hydride and the product heated with acetic anhydride and then hydrolysed with methanolic potassium hydroxide to give 3β : 16α : 21-trihydroxyeburico-7 : 9(11) : 24(28)-triene (IX) which was identical with an authentic sample prepared by the reduction of polyporenic acid C with lithium aluminium hydride (Bowers, Halsall, and Sayer, *loc. cit.*). Similar methods for the formation of the conjugated diene system have been used in the eburicoic acid (Gascoigne, Robertson, and Simes, *loc. cit.*) and the lanosterol (Cavalla and McGhie, *J.*, 1951, 744) series.

These results show that " polyporenic acid B," as isolated from the fungus, is a mixture of 3β : 16α-dihydroxyeburico-8 : 24(28)-dien-21-oic acid (IV) and 3β : 16α-dihydroxyeburico-7 : 9(11) : 24(28)-trien-21-oic acid. The " monoacetate " isolated must be a mixture of the corresponding 3β-monoacetates since oxidation as described above shows that the

free hydroxyl group is attached to a five-membered ring. The isolation of the 3β-acetate of a fungal acid has been previously reported, both Lahey and Strasser (*J.*, 1951, 873)



and Gascoigne, Holker, Ralph, and Robertson (*J.*, 1951, 2346) having isolated eburicoic acid 3β-monoacetate from *P. anthracoplulus* Cooke grown naturally on *Eucalyptus regnans*.

Experimental

Rotations were determined in chloroform at room temperature unless otherwise stated. M.p.s were determined on a Kofler block and are corrected. The alumina used for chromatography, unless otherwise stated, was Peter Spence grade 'H' and had been deactivated with 5% of 10% acetic acid solution. Light petroleum refers to the fraction with b. p. 60—80°. Ultra-violet spectra were determined in ethanol.

Isolation from Polyporus betulinus *Fr. of Polyporenic Acid B and its* 3β-*Monoacetate as their Methyl Esters.*—Minced fungus (ca. 5 kg.), which had already been extracted twice with ethanol to remove polyporenic acid A, was extracted with acetone. The extract was methylated with ethereal diazomethane and then separated into ketonic and non-ketonic fractions by use of Girard's reagent T, the former fraction containing methyl polyporenate C. The non-ketonic fraction (50 g.) was adsorbed from light petroleum (200 c.c.) on alumina (1000 g.) which had been deactivated with aqueous acetic acid (10%; 100 g.). Elution with light petroleum (1000 c.c.; 1000 c.c.; 1500 c.c.) and with benzene (500 c.c.; 2500 c.c.) gave the following five fractions: (i) orange oil (12·3 g.), (ii) white gummy solid (4·4 g.), (iii) yellow gum (4·0 g.), (iv) brown gum (12·4 g.), and (v) brown gum (5·9 g.). Fraction (ii) was washed with light petroleum and crystallised from methanol, giving needles (1·2 g.), m. p. 173—178°. Fractions (iii) and (iv) were crystallised from methanol, giving ergosterol (0·3 g. and 1·2 g.), m. p. 142—148°. The mother liquors from fractions (iii) and (iv), and fraction (v) were combined and rechromatographed on alumina (600 g.) to give, with the solvents indicated, the following brown gums: (1) with benzene (250 c.c.) (0·7 g.), (2) with benzene (750 c.c.) (1·3 g.), (3) with benzene (750 c.c.) (0·7 g.), (4) with benzene–ether (9 : 1; 750 c.c.) (2·7 g.), (5) with benzene–ether (9 : 1; 1750 c.c.) (2·5 g.), and (6) with benzene–ether (1 : 1; 500 c.c.) (1·5 g.).

Fraction (2) was crystallised from methanol, giving the *monoacetate* of "*methyl polyporenate B*" as needles (0·8 g.), m. p. 175—180°, raised by further crystallisations from methanol to 180—184°, $[\alpha]_D$ +39° (*c*, 1·1) (Found: C, 75·45; H, 10·2. $C_{34}H_{54}O_5$ requires C, 75·25; H, 10·05. $C_{34}H_{52}O_5$ requires C, 75·5; H, 9·7%). Light absorption: Max., 2360, 2430, and 2520 Å; ε = 2160, 2420, and 1640.

Fraction (5) was crystallised from methanol, giving "methyl polyporenate B" as needles (1·5 g.), m. p. 160—165°, raised by further crystallisations from methanol to 168—171°, $[\alpha]_D$ +28° (*c*, 1·01) (Found: C, 76·85; H, 10·15. Calc. for $C_{32}H_{52}O_4$: C, 76·75; H, 10·45. Calc. for $C_{32}H_{50}O_4$: C, 77·05; H, 10·1%). Light absorption: Max., 2360, 2430, and 2520 Å; ε = 5250, 6500, and 3550.

Hydrolysis of fraction (2) and also fraction (ii) from the first chromatogram with methanolic

potassium hydroxide yielded " methyl polyporenate B," m. p. 160—165°, $[\alpha]_D$ +27° (*c*, 0·97). Fraction (ii) is therefore the monoacetate.

The mother liquor from fraction (2), and fractions (3) and (4) contained a mixture of " methyl polyporenate B " and its monoacetate. Hydrolysis of these fractions with 5% methanolic potassium hydroxide for 16 hr. at 20°, followed by purification of the product, yielded " methyl polyporenate B " (1 g.).

Acetylation of " Methyl Polyporenate B."—The ester (m. p. 160—165°; 0·6 g.) was treated with acetic anhydride (10 c.c.) and pyridine (10 c.c.) at 100° for 4 hr. The product was crystallised several times from methanol, giving the *diacetate* as needles (0·4 g.), m. p. 159—161°, $[\alpha]_D$ +10·5° (*c*, 0·99) (Found : C, 73·9; H, 9·8. $C_{36}H_{56}O_6$ requires C, 73·95; H, 9·65. $C_{36}H_{54}O_6$ requires C, 74·2; H, 9·35%). Light absorption : Max., 2360, 2430, and 2510 Å; ε = 3420, 3930, and 2580.

Acetylation of " Methyl Polyporenate B Monoacetate " Isolated from the Fungus.—The monoacetate (0·4 g.) was treated with acetic anhydride (5 c.c.) and pyridine (5 c.c.) at 100° for 4 hr. The product was adsorbed on alumina (20 g.) and eluted with benzene (300 c.c.), giving the diacetate as needles (250 mg.) (from methanol), m. p. 155—158° undepressed on admixture with a sample prepared from " methyl polyporenate B," $[\alpha]_D$ +10° (*c*, 1·02). Light absorption : Max., 2360, 2430, and 2510 Å; ε = 3300, 3740, and 2340.

Oxidation of " Methyl Polyporenate B Monoacetate " Isolated from the Fungus.—An aqueous sulphuric acid solution of chromic acid (6N; 0·6 c.c.) was added to a solution of the monoacetate (200 mg.) in acetone (10 c.c.). The mixture was immediately diluted with water and extracted with ether. The extract was adsorbed from benzene on alumina (10 g.). Elution with benzene (200 c.c.) gave the *monoketone* as needles (from methanol) (150 mg.), m. p. 175—177°, $[\alpha]_D$ −42° (*c*, 1·0) (Found : C, 75·35; H, 9·7. $C_{34}H_{52}O_5$ requires C, 75·5; H, 9·7. $C_{34}H_{50}O_5$ requires C, 75·8; H, 9·35%). Light absorption : Max., 2360 and 2430 Å; inflexion, 2510 Å; ε = 2540, 2750, and 2020.

Oxidation of " Methyl Polyporenate B."—" Methyl polyporenate B " (100 mg.) was oxidised as in the experiment described above. The product was adsorbed from benzene on alumina (5 g.) and eluted with benzene, giving the *diketone* as plates (from methanol) (70 mg.) m. p. 155—157°, $[\alpha]_D$ −62° (*c*, 1·03) (Found : C, 77·6; H, 9·45. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·75. $C_{32}H_{46}O_4$ requires C, 77·7; H, 9·4%). Light absorption : Max., 2360 and 2430 Å; inflexion, 2510 Å; ε = 5620, 6200, and 4120.

Hydrogenation of " Methyl Polyporenate B."—The ester (1·3 g.) in ethanol (125 c.c.) was shaken with hydrogen at 20° in the presence of Adams's catalyst (100 mg.) until the uptake of hydrogen ceased. The product was crystallised from methanol, giving the *dihydro*-derivative as needles (900 mg.), m. p. 173—174°, $[\alpha]_D$ +25° (*c*, 0·98) (Found : C, 76·55; H, 11·0. $C_{32}H_{54}O_4$ requires C, 76·45; H, 10·85. $C_{32}H_{52}O_4$ requires C, 76·75; H, 10·45%). Light absorption : Max., 2360, 2430, and 2520 Å; ε = 4850, 6100, and 3220.

Conversion of " Methyl Dihydropolyporenate B " into Methyl 3β : 16α-*Dihydroxyeburico*-7 : 9(11)-*dien*-21-*oate* (VI).—The dihydro-ester (400 mg.) in ether (100 c.c.) was added to an ethereal solution of monoperphthalic acid (15 c.c.; 10 mols.), and the mixture kept at 20° for 5 days. The ethereal solution was then washed with sodium hydrogen carbonate solution and with water, dried, and evaporated to dryness. The crude epoxide (300 mg.) in ethanol (50 c.c.) was heated under reflux with concentrated hydrochloric acid (2 c.c.) for 3 hr. Dilution with water and isolation with ether yielded a product which was adsorbed on alumina (15 g.). Elution with benzene–ether (4 : 1; 200 c.c.) afforded methyl 3β : 16α-dihydroxyeburico-7 : 9(11)-dien-21-oate as needles (150 mg.), m. p. 189—190° (two crystallisations from methanol), undepressed on admixture with an authentic sample {m. p. 188—190°, $[\alpha]_D$ +24° (Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548)}, $[\alpha]_D$ +27° (*c*, 0·94) (Found : C, 74·15; H, 10·4. Calc. for $C_{32}H_{52}O_4,CH_3{\cdot}OH$: C, 74·4; H, 10·6%). Light absorption : Max., 2360, 2430, and 2520 Å; ε = 14,000, 16,500, and 10,900.

Conversion of " Methyl Polyporenate B Diacetate " into 3β : 16α : 21-*Trihydroxyeburico*-7 : 9(11) : 24(28)-*triene* (IX).—The diacetate (900 mg.) was oxidised in acetic acid (50 c.c.) with chromic acid (450 mg.) at 80—90° for 10 min. After dilution with water, isolation with ether yielded a product which was adsorbed on alumina (50 g.). Elution with benzene (200 c.c.) gave a gum (15 mg.) which was discarded. Further elution with benzene–ether (9 : 1; 600 c.c.) afforded a gum (350 mg.) which showed maximum light absorption in ethanol at 2540 Å, indicative of the presence of methyl 3β : 16α-diacetoxy-7-oxoeburico-8(9) : 24(28)-dien-21-oate. The gum was dissolved in ether (100 c.c.) and heated under reflux with lithium aluminium hydride (900 mg.) for 3 hr. Decomposition of the complex with dilute sulphuric acid and isolation with

ether yielded a white solid which was heated under reflux with acetic anhydride (50 c.c.) for 1 hr. Dilution with water and extraction with ether afforded a gum which was heated under reflux with methanolic potassium hydroxide (10%; 50 c.c.) for 30 min. The product (250 mg.) was adsorbed from benzene–ether (9 : 1; 50 c.c.) on alumina (10 g.); elution with benzene–ether (4 : 1; 70 c.c.) gave an impure fraction (50 mg.). Further elution with this solvent (300 c.c.) afforded 3β : 16α : 21-trihydroxyeburico-7 : 9(11) : 24(28)-triene as needles (190 mg.), m. p. and mixed m. p. 218—219° (two crystallisations from methanol), $[\alpha]_D$ +34° (*c*, 0·78 in pyridine). Light absorption: Max., 2360, 2430, and 2520 Å; ε = 15,000; 17,400, and 11,600.

The authors thank Mr. E. S. Morton and Mr. H. Swift for the microanalyses. Two of the authors (J. M. G. and R. H.) are indebted, respectively, to the Department of Scientific and Industrial Research for a maintenance grant and to the Royal Commissioners of the 1851 Exhibition for the award of an Overseas Scholarship. The assistance of Mr. A. Bowers is gratefully acknowledged. Infra-red spectra were determined under the direction of Dr. G. D. Meakins.

THE UNIVERSITY, MANCHESTER, 13. [*Received, May 5th,* 1954.]

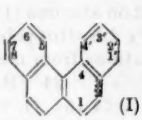
Substituted Anthracene Derivatives. Part VIII. The Conjugating Powers of the Substitution Positions in* 3 : 4*-Benzophenanthrene.*

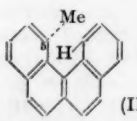
By G. M. BADGER and I. S. WALKER.

[Reprint Order No. 5229.]

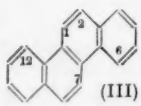
The absorption spectra of 3 : 4-benzophenanthrene (I) and of its six monomethyl derivatives have been examined. The bathochromic shifts produced by methyl substitution have been compared with the conjugating powers of the six substitution positions calculated by the method of molecular orbitals.

METHYL substitution in benzenoid aromatic hydrocarbons normally produces a shift in the ultra-violet absorption bands to longer wave-lengths, the extent of the bathochromic shift depending on the degree of electronic interaction between the substituent and the ring (Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127; *Chem. Reviews*, 1943, **32**, 1; Doub and Vandenbelt, *J. Amer. Chem. Soc.*, 1947, **69**, 2714). Many of the polycyclic compounds have several positions available for substitution, and in the case of 1 : 2-benzanthracene an attempt has already been made to estimate the relative conjugating abilities of the various positions by measuring the bathochromic shifts produced by methyl substitution (Badger, Pearce, and Pettit, *J.*, 1952, 1112). Although this method is only very approximate, the greatest shifts are produced by methyl substitution at positions of greatest self-polarisability as calculated by the method of molecular orbitals. We have therefore now examined the absorption spectra of 3 : 4-benzophenanthrene (I) and of all six possible monomethyl derivatives.


(I)



(II)


(III)

The bands in the absorption spectrum of 3 : 4-benzophenanthrene (see Figure) fall into three main groups: group I, bands *A*—*E*; group II, bands *F*—*I*; group III, bands *J*—*L*. All the monomethyl derivatives show similar absorption spectra (see Table 1) except that the bands are shifted to somewhat longer wave-lengths, and in some cases (notably 5-methyl-3 : 4-benzophenanthrene) there is a certain loss of fine structure. For the two most prominent bands (*E* and *H*) the bathochromic shifts are given in Table 2.

According to Coulson and Longuet-Higgins (*Proc. Roy. Soc.*, 1947, *A*, **191**, 39; 1948, *A*, **195**, 188), the conjugating power of a given position is defined as β times the self-polarisa-

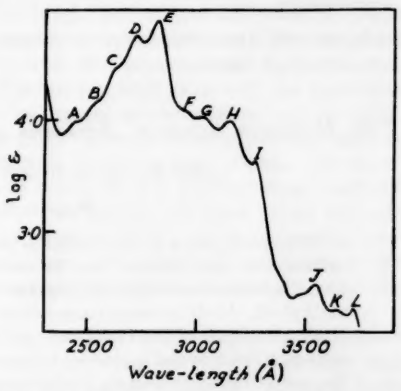
* Part VII, *J.*, 1954, 3151.

TABLE 1. *Positions of the maxima and corresponding intensities* (log $\varepsilon_{max.}$) *in the ultra-violet absorption spectra of* **3** : **4**-*benzophenanthrene and of the methyl-***3** : **4**-*benzophenanthrenes (in ethanol).**

Position of Me	*A*	*B*	*C*	*D*	*E*	*F*	*G*	*H*	*I*	*J*	*K*	*L*
†	(2450)	(2540)	(2635)	2715	2815	(2945)	3020	3145	3265	3545	3630	3720
	3·99	4·16	4·48	4·76	4·90	4·09	4·03	4·00	3·63	2·52	2·29	2·30
1	(2460)	(2545)	(2655)	2745	2835	2985	(3045)	3160	(3270)	3590	—	3770
	4·02	4·16	4·45	4·71	4·83	4·16	4·09	4·01	3·62	2·57	—	2·41
2	2455	2545	(2650)	2735	2835	(2955)	3050	3175	3300	3565	—	3745
	4·00	4·14	4·43	4·74	4·89	4·10	4·02	4·01	3·71	2·60	—	2·38
5	—	—	—	2775	2865	(3000)	3085	3210	(3330)	3625	—	—
	—	—	—	4·73	4·83	4·08	3·99	3·95	3·67	2·49	—	—
6	2470	(2550)	(2645)	2735	2830	2990	(3035)	3160	(3265)	3570	—	3750
	4·00	4·17	4·45	4·72	4·85	4·14	4·09	4·00	3·60	2·72	—	2·65
7	(2465)	(2540)	(2640)	2730	2830	(2955)	3035	3160	(3275)	3560	—	3735
	4·00	4·14	4·43	4·75	4·91	4·08	4·03	4·01	3·64	2·54	—	2·26
8	(2480)	(2575)	(2670)	2760	2855	(2970)	3055	3180	3300	3575	(3655)	3745
	4·03	4·23	4·49	4·73	4·84	4·18	4·06	4·00	3·69	2·51	2·33	2·19

* Figures in parentheses are points of inflexion. † Parent compound.

bility of that position. The self-polarisabilities for the various positions in **3** : 4-benzophenanthrene have now been calculated, a simplified mathematical technique being used (Potts, *J. Chem. Phys.*, 1953, **21**, 758; Potts and Walker, unpublished work), and are



Absorption spectrum of **3** : **4**-*benzophenanthrene in ethanol.*

included in Table 2, together with the free valence numbers for the various positions. As in other cases (Badger, Pearce, and Pettit, *loc. cit.*) there is a satisfactory linear relation between the self-polarisabilities and the free valence numbers, so that either set of figures may be used to estimate relative conjugating abilities. Unfortunately the bathochromic

TABLE 2. *Bathochromic shifts (E and H bands) for methyl substitution, calculated conjugating powers, and free valence numbers for* **3** : **4**-*benzophenanthrene.*

Position	ΔE (Å)	ΔH (Å)	Self-polarisability [a] (M.O. method)	Free valence number M.O. method [b]	V.B. method [c]
6	15	15	0·408	0·089	0·173
7	15	15	0·409	0·086	0·167
5	50	65	0·435	0·127	0·190
1	20	15	0·438	0·131	0·202
8	40	35	0·440	0·132	0·196
2	20	30	0·442	0·133	0·208

[a] These values should be multiplied by $1/\beta$. [b] Based on $N_{max.} = 3 + \sqrt{2}$; cf. Berthier, Coulson, Greenwood, and Pullman, *Compt. rend.*, 1948, **226**, 1906. [c] Pullman, *Ann. Chim.*, 1947, **2**, 5.

shifts produced by methyl substitution in 3 : 4-benzophenanthrene are rather small, and the results must therefore be interpreted with caution. However, in agreement with the theoretical work, it seems that the 2- and the 8- have greater conjugating powers than the 6- and the 7-position. On the other hand, the greatest bathochromic shift was produced by

5-methyl substitution, though the self-polarisability and the free valence numbers indicate only moderate conjugating power. In 5-methyl-3 : 4-benzophenanthrene (II) the methyl substituent cannot be in the plane of the ring system (Newman and Wheatley, *J. Amer. Chem. Soc.*, 1948, **70**, 1913) and there seems little doubt that the anomalous bathochromic shift is associated with this fact. Several other cases have been recorded in the literature where methyl groups which are not coplanar with the ring system have been shown to give very large bathochromic shifts. For example, very large shifts are produced in 1-methyl-, 6-methyl-, and 1 : 12-dimethyl-chrysene (III), and a large shift is also evident for 4 : 5-dimethylphenanthrene (Brode and Patterson, *J. Amer. Chem. Soc.*, 1941, **63**, 3252; Jones, *ibid.*, 1941, **63**, 313; Friedel and Orchin, "Ultra-violet Spectra of Aromatic Compounds," Wiley, 1951; see also Brockmann and Dorlars, *Chem. Ber.*, 1952, **85**, 1168). However, more data are required, for 1'-methyl substitution in 1 : 2-benzanthracene produces only a very small bathochromic shift and steric hindrance must be involved also in this case.

Experimental

Spectra.—Spectra were determined, in absolute ethanol, with a Hilger Uvispek Spectrophotometer. The positions of the peaks were checked by examination of the spectra in hexane. Little if any solvent effect was apparent.

We are very grateful to Professor Melvin S. Newman for gifts of all the compounds used in this investigation.

University of Adelaide, South Australia. [*Received, March 23rd*, 1954.]

The Reaction between Acridine and Methyl Acetylenedicarboxylate.

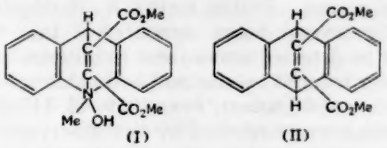
By R. M. Acheson and M. L. Burstall.

[Reprint Order No. 5318.]

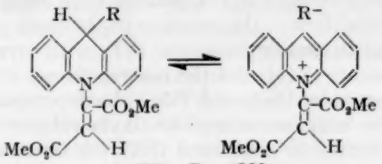
Reinvestigation of the reaction between acridine and methyl acetylenedicarboxylate has shown that in methanol the product is largely 10-(*trans*-1 : 2-dimethoxycarbonylvinyl)acridinium methoxide, but that in ether methyl 5 : 10-dihydro-5-oxoacridinyl-fumarate and -maleate are formed. Hydrogenolysis of the fumarate yielded acridone and methyl fumarate. The configurations of the acridone derivatives were established by conversion into the anhydride followed by hydrolysis, which gives only the *cis*-acid.

Although many reagents are known to add to the 9 : 10-positions of anthracene comparatively few addition reactions of acridine have been systematically investigated. Acridine is reported (Barnett, Goodway, Higgins, and Lawrence, *J.*, 1934, 1224) not to react with maleic anhydride but gives, according to Diels and Thiele (*Annalen*, 1939, **543**, 79), largely the adduct (I) with methyl acetylenedicarboxylate in the presence of methanol. This structure was presumably based on that of the anthracene–methyl acetylenedicarboxylate adduct (II) (Diels and Alder, *Annalen*, 1931, **486**, 191). Possible alternative structures for the latter adduct, which are also consistent with the chemical degradations, those of methyl 9-anthryl-fumarate or -maleate, were not considered by these workers; they have now been excluded as the ultra-violet absorption of the adduct is compatible with the 9 : 10-dihydroanthracene (cf. Phillips and Cason, *J. Amer. Chem. Soc.*, 1952, **74**, 2934), but not with the anthracene, formulation. The bright red acridine adduct, formulated as (I), was obtained by Diels and Thiele in 80—90% yield, along with 2—3% of a yellow isomer. The red compound was reported to contain three methoxyl groups, and on mild oxidation to give (VI), containing two methoxyl groups. Only one of the methoxyl groups in the bright red adduct was replaced by an ethoxyl group simply on crystallisation from ethanol. These observations cannot be explained satisfactorily by the structure (I) given by Diels and Thiele, and it was thought that the bright red adduct was probably (III) on the basis of which the experimental data can be explained.

Repetition of the acridine–methyl acetylenedicarboxylate reaction in methanol gave the bright red compound in high yield but we were unable to isolate any yellow isomer. The ultra-violet absorption spectrum of this adduct was of the acridinium-ion type in neutral methanol, and of the 5-methoxyacridan type after the addition of potassium



(I) (II)

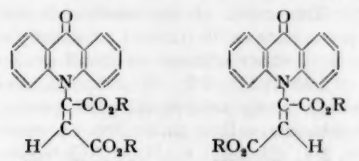


(III): R = OMe
(IV): R = OEt

hydroxide. As this behaviour was similar to that of 10-methylacridinium chloride (cf. Tinkler, *J.*, 1906, **856**) structure (III) was confirmed. Recrystallisation of the adduct from ethanol gave another red compound (IV), which was also obtained when the original addition reaction was carried out in ethanol, and both the compounds (III) and (IV) with picric acid gave the same quaternary picrate showing that both were in equilibrium with an acridinium ion. This ready exchange of 5-alkoxyl groups is characteristic of the 5-alkoxy-10-alkylacridans (Decker, *Ber.*, 1902, **35**, 3068).

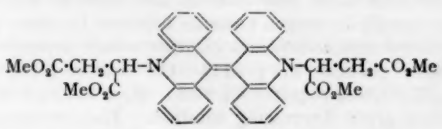
Diels and Thiele (*loc. cit.*) claimed that the bright red adduct (III) was degraded by concentrated hydrochloric acid to 10-methylacridinium chloride, but this could not be confirmed. Degradation of the adduct (III) with hot concentrated hydrochloric acid, methanolic hydrogen chloride, or concentrated sulphuric acid gave only the corresponding salts of acridine in 20—60% yield. Further, treatment of the ethanol adduct (IV) with hot ethanolic hydrogen chloride gave acridine hydrochloride although 10-ethylacridinium chloride would have been expected from Diels and Thiele's observations. No trace of a 10-alkylacridinium salt or 10-alkylacridone was detected as a product from any of these degradations. Both compounds (III) and (IV) were readily oxidised by air or hydrogen peroxide in neutral solution to the orange acridone ester (VIII). This behaviour is typical of 5-alkoxy-10-alkylacridans (cf. Decker, *J. pr. Chem.*, 1892, **45**, 161). Alkaline hydrolysis of the acridan (III) was also accompanied by aerial oxidation and gave the acridone acid (VII).

The ultra-violet absorption spectrum of the acridone ester (VIII) closely resembled that of acridone. Both compounds also showed the same infra-red absorption maxima (6·10 μ), which may be characteristic of the acridone-carbonyl group. Alkaline hydrogen peroxide oxidised the orange ester (VIII) to acridone itself, showing that the aliphatic part of the molecule was attached to the heterocyclic nitrogen atom; a small yield of acridone was also obtained from the acid (VII) and potassium permanganate in cold acetone, but much of the acid was recovered. These results were unexpectedly confirmed by the interesting hydrogenolysis of the ester (VIII) in ethanol over freshly prepared Raney nickel to acridone and methyl fumarate. This reaction, which does not appear to have any parallel, took place very readily at room temperature and atmospheric pressure. The orange acridone (VIII), in contrast to the acridinium methoxide (III), gave only a mixture of half esters with hot concentrated sulphuric acid.



(V): R = H
(VI): R = Me

(VII): R = H
(VIII): R = Me



(IX)

Diels and Thiele (*loc. cit.*) reported that acridine and methyl acetylenedicarboxylate reacted in ether to give a mixture of the orange acridone (VIII), a creamy-white geometric

isomer (VI) [stated erroneously to be (VI) and (VIII) respectively], and a third compound alleged to be formed from one molecule of acridine and two of the ester. Repetition of this experiment gave roughly equal amounts of the first two adducts in *ca.* 40% total yield but we were unable to confirm the formation of the third adduct. The ultra-violet absorption spectra of the two compounds were almost indistinguishable and the infra-red absorption spectra showed the presence of the same principal groups. Boiling methyl 5 : 10-dihydro-5-oxo-10-acridinylmaleate (VI) with pyridine for several hours converted it into the fumarate (VIII) but the reverse change could not be detected under these conditions. As reported by Diels and Thiele, both compounds were reduced by zinc and hydrochloric acid in the usual manner of 10-alkylacridones (cf. Decker and Dunant, *Ber.*, 1909, **42**, 1176) to the binuclear compound (IX), the structure of which was confirmed by two observations. The ultra-violet absorption spectrum of the solution obtained by oxidising it with dilute nitric acid showed a close resemblance to that of 10 : 10′-dimethyl-5 : 5′-diacridinium dinitrate, and the oxidised solution, presumably containing 10 : 10′-di-(1 : 2-dimethoxycarbonylethyl)-5 : 5′-diacridinium dinitrate, gave an intense blue chemiluminescence with alkaline 30% hydrogen peroxide. This is characteristic of most 10 : 10′-dialkyl-5 : 5′-diacridinium dinitrates (Gleu and Nitzsche, *J. pr. Chem.*, 1939, **153**, 233).

The stereochemistry of the compounds was established as follows. The dibasic acids (V) and (VII), gave the same anhydride when heated with acetic anhydride. As this anhydride was converted into the dicarboxylic acid (V) on hydrolysis with warm alkali, the white adduct must have the *cis*- (VI) and the orange acridone (VIII) the *trans*-configuration. The possibility that stereochemical rearrangement had taken place during the alkaline hydrolysis of the esters was eliminated by reconversion of the acids into the original esters by treatment with diazomethane.

The structures of the compounds obtained in these addition reactions suggest that the reactions are closely analogous to Michael additions which are well known to take place with acetylenedicarboxylic esters, and to give mainly *trans*-adducts (cf. A. W. Johnson, "Acetylenic Acids," Edward Arnold and Co., London, 1950). This behaviour contrasts with the quite different behaviour of pyridine, quinoline, and *iso*quinoline, which react with acetylenedicarboxylic esters to give pyrrocoline and pyridocoline derivatives (Johnson, *loc. cit.*). It is possible that the blocking of both carbon atoms α- to the nitrogen atom inhibits cyclisation to pyrrocolines, etc., but on the other hand such products must arise from the reaction of one molecule of the base with two of the ester, and no compounds of this type, either cyclised or otherwise, were obtained from acridine under the conditions used in this investigation.

Experimental

Methyl 9 : 10-dihydroanthracene-9 : 10-*endo*maleate (II), prepared according to Diels and Alder (*Annalen*, 1931, **486**, 191), had m. p. 160° (Found : C, 75·3; H, 5·1. Calc. for $C_{20}H_{16}O_4$: C, 75·0; H, 5·0%). In methanol it showed $\lambda_{max.}$ 2700 (log ε 3·36) and 2800 Å (log ε 3·34).

10-(trans-1 : 2-*Dimethoxycarbonylvinyl*)*acridinium Methoxide* (III).—Acridine (7·5 g.), methyl acetylenedicarboxylate (5·0 ml.), and methanol (30 ml.) were refluxed from a steam-bath for 3 hr. The deep red solid which separated at 0° crystallised from methanol, giving the *acridinium methoxide* (III) as ruby-red rhombs (12·0 g.), m. p. 101—102° (Found : C, 68·3; H, 5·4; N, 4·0. $C_{20}H_{19}O_5N$ requires C, 68·0; H, 5·4; N, 4·0%). In neutral methanol it showed $\lambda_{max.}$ 2600, 3600, and 4300 Å (log ε 4·64, 4·36, and 3·61), and after the addition of sodium hydroxide 2720 (log ε 4·32) and 3150 Å (log ε 3·63). Treatment of the methoxide with methanolic hydrogen chloride followed by ether gave a precipitate of 10-(trans-1 : 2-*dimethoxycarbonylvinyl*)*acridinium chloride* which separated from 1 : 1 ether–ethanol as small orange-yellow rhombs, m. p. 114—116° (decomp.) (Found : C, 63·6; H, 4·7; N, 3·9; Cl, 10·1. $C_{19}H_{16}O_4NCl$ requires C, 63·8; H, 4·5; N, 3·9; Cl, 9·9%), freely soluble in water giving a yellow green fluorescing solution. The corresponding *perchlorate*, yellow plates (from acetone), m. p. 215—216° (decomp.) (Found : C, 54·2; H, 4·1; N, 3·3; Cl, 8·4. $C_{19}H_{16}O_8NCl$ requires C, 54·2; H, 3·9; N, 3·3; Cl, 8·4%), and *picrate*, orange-yellow needles (from methanol), m. p. 185—186° (decomp.) (Found : C, 54·6; H, 3·4; N, 10·3. $C_{25}H_{18}O_{11}N_4$ requires C, 54·6; H, 3·3; N, 10·2%), were prepared similarly.

The acridinium methoxide (III) (1·0 g.) was dissolved in 7N-methanolic hydrogen chloride

and evaporated to dryness on a steam-bath. The black residue, on crystallisation from dilute hydrochloric acid, gave yellow needles of acridine hydrochloride (Found, after drying at 120° : Cl, 16·6. Calc. for $C_{13}H_{10}NCl$: Cl, 16·5%) which on basification gave acridine (0·29 g., 58%), m. p. and mixed m. p. 109°, also identified as *picrate*, m. p. and mixed m. p. 258—259° (decomp., bath initially at 250°) (Found : C, 56·1; H, 3·0; N, 13·5. $C_{19}H_{12}O_7N_4$ requires C, 55·9; H, 2·9; N, 13·7%) [the usual literature value, 208° (Albert, "The Acridines," p. 128, Edward Arnold and Co., London, 1951) is incorrect]. Similar degradations of the acridinium methoxide (III) (1·0 g.) with hydrochloric acid (36%) at 150° (2 hr.) and with concentrated sulphuric acid at 100° (several hours) gave 0·27 and 0·1 g. of acridine respectively.

The acridinium methoxide (III) (1·0 g.), potassium hydroxide (0·5 g.), water (5 ml.), and methanol (5 ml.) were refluxed for 2 hr. The oil, precipitated on acidification, solidified when warmed. Crystallisation from aqueous ethanol gave 5 : 10-*dihydro*-5-*oxo*-10-*acridinylfumaric acid* (VII) as feathery yellow needles, m. p. 254—255° (decomp.) (Found : C, 66·2; H, 3·8; N, 5·0. $C_{17}H_{11}O_5N$ requires C, 66·0; H, 3·6; N, 4·5%).

10-(trans-1 : 2-*Dimethoxycarbonylvinyl*)*acridinium Ethoxide* (IV).—Acridine (2·0 g.), methyl acetylenedicarboxylate (1·4 ml.), and ethanol (10 ml.) were refluxed for 2 hr. On cooling of the solution in a refrigerator a red syrup separated which on trituration with more ethanol solidified. Crystallisation from ethanol gave the *ethoxide* (IV) as crimson rhombs, m. p. 70—71° (Found : C, 68·2; H, 5·9; N, 3·3. $C_{21}H_{21}O_5N$ requires C, 68·5; H, 5·7; N, 3·8%). In ethanol it showed $\lambda_{max.}$ 2550, 3600, and 4300 Å (log ε 4·65, 4·31, and 3·54). On crystallisation from methanol it yielded the methoxide (III), red rhombs, m. p. and mixed m. p. 101—102°. With ethanolic picric acid the ethoxide (IV) gave the picrate, m. p. 185—186° (decomp.) alone or mixed with the picrate obtained from the methoxide (III); the infra-red absorption spectra of the two picrates in paraffin paste were identical.

Evaporation of the ethoxide (1·0 g.) with ethanolic hydrogen chloride, as for (III) above, gave only acridine (0·29 g., 60%), identified by a mixed m. p. determination and as picrate.

Methyl 5 : 10-*Dihydro*-5-*oxo*-10-*acridinylfumarate*.—(*a*) A solution of the methoxide (III) in methanol or benzene became brown after a few weeks in air at room temperature. The residue obtained on evaporation was dissolved in a little methanol and refrigerated; the *fumarate* (VIII) slowly separated as orange rhombs, m. p. 141—142° (fast heating), m. p. 160—161° (slow heating) with a transition point at 138—139° (Found : C, 67·5; H, 4·6; N, 3·6; OMe, 18·5. $C_{19}H_{15}O_5N$ requires C, 67·7; H, 4·4; N, 4·1; OMe, 18·3%). The ultra-violet absorption spectrum in methanol showed $\lambda_{max.}$ 2550, 3750, and 3900 Å (log ε 4·66, 4·08, and 4·11). The infra-red absorption spectrum in paraffin paste showed strong maxima at 5·76 (ester-carbonyl) and 6·09 μ (acridone-carbonyl).

Unlike the methoxide, the ethoxide (IV) was rapidly oxidised by air in the solid state (the *iso*propoxide could not be obtained pure because of this very ready oxidation). The product obtained after 14 days' exposure to air gave likewise the methyl fumarate when purified chromatographically over alumina from benzene.

(*b*) The acridinium methoxide (III) (5·0 g.), aqueous hydrogen peroxide (3·0 ml.; 30%), and methanol (30 ml.) were refluxed (1 hr.). After evaporation the residue was extracted with hot ethyl acetate. The insoluble material (50 mg.) was acridone, m. p. and mixed m. p. 350°. The brown solid obtained on cooling of the ethyl acetate solution, when crystallised from methanol, yielded the methyl fumarate, identical with the specimen described above. No trace of the deep red by-product, $C_{38}H_{30}O_8N_2$, claimed by Diels and Thiele, could be found. Similar results were obtained when the methoxide (III) was replaced by the ethoxide (IV).

(*c*) The acridone (VIII), or Diels and Thiele's "orange adduct," was best prepared according to their directions. A trace of the maleate (VI) was also formed.

(*d*) The maleate (VI) was refluxed with pyridine for several hours, then poured into excess of dilute aqueous acid. The fumarate (VIII), identical with an authentic specimen, was precipitated.

Hydrolysis of methyl 5 : 10-dihydro-5-oxo-10-acridinylfumarate with boiling methanolic potassium hydroxide (2 hr.), followed by acidification, gave the corresponding acid (VII), which separated from dilute aqueous ethanol as golden needles, m. p. 254—255° (decomp.) (Found : C, 66·0; H, 3·5; N, 4·2%), mentioned above.

Heating the methyl fumarate (1·0 g.) with concentrated sulphuric acid (6 ml.) on a steam-bath for 3 hr. gave an orange solution which was poured into water. The yellow precipitate was collected and on fractional crystallisation from dilute aqueous ethanol gave a mixture of hydrogen esters. The more soluble *ester* crystallised in fine orange needles, m. p. 115—116° (decomp.) (Found : C, 60·1; H, 4·9; N, 4·6. $C_{18}H_{13}O_5N,2H_2O$ requires C, 60·2; H, 4·7; N,

3·3%). The less soluble *ester* separated in small pale-yellow rhombs, m. p. 247—248° (decomp.) (Found: C, 66·4; H, 4·2; N, 4·5. $C_{16}H_{13}O_5N$ requires C, 66·8; H, 4·0; N, 4·3%). Both half-esters with diazomethane in ether gave the original diester (VIII).

Degradation of Methyl 5 : 10-*Dihydro*-5-*oxo*-10-*acridinylfumarate to Acridone.*—(*a*) The ester (0·2 g.), aqueous hydrogen peroxide (30%; 3 ml.), and methanol (3 ml.) were refluxed for several hours but there was no change in colour. The addition of some aqueous sodium hydroxide (2N), however, caused a vigorous reaction with the evolution of much oxygen. The solution developed a strong blue fluorescence. The solution was cooled and the yellow precipitate, after crystallisation from much ethanol, yielded acridone (50 mg.), m. p. 350° (Found: C, 79·8; H, 4·9. Calc. for $C_{13}H_9ON$: C, 80·0; H, 4·6; N, 7·2%).

(*b*) The ester (1·0 g.) in ethanol (50 ml.) was shaken with hydrogen over fresh Raney nickel at atmospheric pressure and temperature. After one mol. of hydrogen had been taken up (15 min.) the solution was filtered and the filtrate largely evaporated. It deposited pale yellow needles of acridone (0·3 g.), m. p. 350° (Found: C, 79·7; H, 4·8; N, 7·0%). The mother-liquor was evaporated and the residue distilled at atmospheric pressure on to a cold finger. The yellow sublimate on crystallisation from methanol gave colourless needles of methyl fumarate, m. p. and mixed m. p. 102°.

Methyl 5 : 10-*Dihydro*-5-*oxo*-10-*acridinylmaleate* (VI).—Acridine (2·0 g.), methyl acetylenedicarboxylate (1·4 ml.), and ether (20 ml.) were kept together at room temperature for 2 days. Evaporation of the orange solution and trituration with methanol gave a red solid, which on crystallisation from acetonitrile yielded colourless rhombs of the *maleate* (VI) (0·75 g.), m. p. 222—223° (Found: C, 67·3; H, 4·4; N, 4·7; OMe, 18·3. $C_{19}H_{15}O_5N$ requires C, 67·7; H, 4·4; N, 4·1; OMe, 18·3%). The ultra-violet absorption spectrum in methanol showed $\lambda_{max.}$ 2550, 3740, and 3900 Å (log ε 4·73, 4·02, and 4·06). The infra-red absorption spectrum in paraffin paste showed strong maxima at 5·75 (ester-carbonyl) and at 6·10 μ (acridone-carbonyl). Evaporation of the methanol from the trituration and trituration of the residue with ether gave a buff solid (0·75 g.) which proved to be very largely the fumarate.

5 : 10-*Dihydro*-5-*oxo*-10-*acridinylmaleic acid*, obtained from the ester by reaction with methanolic potassium hydroxide, separated from dilute aqueous ethanol as fine pale yellow needles, m. p. 227—228° (decomp.) (Found, after drying at 120° *in vacuo*: C, 64·5; H, 3·8; N, 4·1. $C_{17}H_{11}O_5N,\frac{1}{2}H_2O$ requires C, 64·2; H, 3·8; N, 4·4%).

5 : 10-*Dihydro*-5-*oxo*-10-*acridinylmaleic Anhydride.*—The fumaric acid (VII) (1·0 g.) and acetic anhydride (1·5 ml.) were refluxed from an oil-bath for 2 hr. On cooling, a brown solid separated. This on crystallisation from acetic anhydride yielded orange-brown rhombs of the *maleic anhydride*, m. p. 231—232° (decomp.) (Found: C, 70·0; H, 3·2; N, 4·6. $C_{17}H_9O_4N$ requires C, 70·0; H, 3·1; N, 4·8%). Treatment of 5 : 10-dihydro-5-oxo-10-acridinylmaleic acid (V) in the same way yielded the same anhydride, m. p. 231—232° (decomp.) (Found: C, 69·9; H, 3·2; N, 4·9%). A mixed m. p. determination with the previous specimen showed no depression and the infra-red absorption spectra (paraffin paste) of the substances were identical and showed large absorption maxima at 5·40 and 5·60 μ.

The anhydride was hydrolysed in warm 2N-sodium hydroxide. Acidification gave a white precipitate which on crystallisation from dilute aqueous ethanol yielded pale yellow needles of the maleic acid, m. p. 227—228° (decomp.) (Found, after drying at 120°: C, 64·3; H, 3·8; N, 4·7%). Treatment of an ethereal suspension of the acid with diazomethane, followed by evaporation and crystallisation of the residue from acetonitrile, gave methyl 5 : 10-dihydro-5-oxo-10-acridinylmaleate as white rhombs, m. p. and mixed m. p. 222—223°.

10 : 10′-*Di*-(1 : 2-*dimethoxycarbonylethyl*)-5 : 5′ : 10 : 10′-*tetrahydro*-5 : 5′-*diacridinylidene* (IX).—The fumarate (VIII) (2·0 g.), zinc dust (1·7 g.), methanol (60 ml.), and concentrated hydrochloric acid (8 ml.) were heated on a steam-bath for 2 hr. After cooling, the green residue was collected and crystallisation from acetonitrile gave green rhombs of the diacridinylidene, m. p. 255° (decomp.) (Found: C, 70·7; H, 5·1; N, 4·3. Calc. for $C_{38}H_{34}O_8N_2$: C, 70·6; H, 5·3; N, 4·3%). Diels and Thiele give m. p. 260° (decomp.). The ultra-violet absorption spectrum in methanol showed $\lambda_{max.}$ 2350, 2650, 2800, 3750, and 4000 Å (log ε 4·27, 4·10, 3·83, 3·71, and 3·75). The ultra-violet absorption spectrum of the (cooled) solution in hot dilute nitric acid showed $\lambda_{max.}$ 2650, 3700, and 4400 Å (log ε 4·71, 4·42, and 3·92).

The same product was obtained when the maleate was treated similarly. It had m. p. 255° (decomp.) alone or mixed with the above specimen and the infra-red absorption spectra (paraffin paste) of the two specimens were identical and showed the ester-carbonyl absorption maximum at 5·76 μ.

10 : 10′-Dimethyl-5 : 5′-diacridinium dinitrate was prepared according to Decker and Petsch

(*J. pr. Chem.*, 1935, **143**, 211). The ultra-violet absorption spectrum showed $\lambda_{max.}$ 2550, 3700, and 4300 Å (log ε 4·85, 4·28, and 3·75).

We thank Mr. F. Hastings for the optical data, which were obtained under the supervision of Dr. F. B. Strauss, and the Director of the Chemical Research Laboratories (Teddington) for a gift of acridine.

THE DYSON PERRINS LABORATORY AND THE LABORATORY OF HUMAN NUTRITION,
OXFORD. [*Received, April 20th*, 1954.]

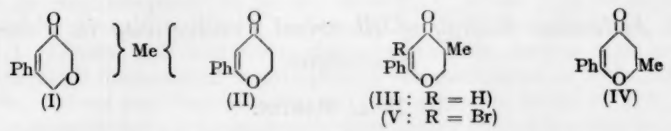
NOTES.

A Constituent of the Essential Oil of Myrtus bullata.

By C. W. BRANDT, W. I. TAYLOR, and B. R. THOMAS.

[Reprint Order No. 5334.]

A READILY crystallised, optically inactive compound, $C_{12}H_{12}O_2$, was isolated from the essential oil of *Myrtus bullata* (Banks and Solander), a shrub endemic to New Zealand and common in the lowland forests of the North Island. The infra-red spectrum (solid film) showed a strong band at 1681 cm.$^{-1}$ in the carbonyl-stretching region suggestive of an αβ-unsaturated ketone group in a six-membered ring, and the ultra-violet absorption showed the presence of the chromophoric grouping Ph·CH:CH·CO· (cf. Wilds *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 1985). Presence of the unsaturated ketone grouping was confirmed by the preparation of a 2 : 4-dinitrophenylhydrazone, which showed a maximum, as expected, at 412 mμ. There was no hydroxyl-stretching absorption at *ca.* 3000 cm.$^{-1}$ and this was supported by negative results on attempted acylation. An ether linkage was therefore inferred and since Zeisel determinations were negative, the second oxygen atom must form part of the six-membered ring containing the ketonic system. This leads to the partial structures (I) and (II) as the only possibilities, with a methyl group, confirmed by *C*-methyl determination, as yet unplaced.



(I) (II) (III : R = H) (V : R = Br) (IV)

On hydrolysis in aqueous-alcoholic potassium hydroxide the compound yielded both acetophenone and benzoic acid which could only have arisen by fission of the potential 1 : 3-diketone in the 2 : 3-dihydro-δ-pyrone (II). The formation of acetophenone instead of propiophenone showed that the methyl group could not be at $C_{(3)}$; thus the only structures available are (III) and (IV). A decision between them was readily made since the dihydropyrone was stable to selenium dioxide in boiling acetic acid, and therefore the compound must be (III) with no methylene group adjacent to the carbonyl group.

To provide further support, attempts were made to dehydrogenate or oxidise the dihydropyrone to the pyrone, but without success. Addition of one mol. of bromine in carbon tetrachloride followed by debromination afforded a compound, $C_{12}H_{11}O_2Br$, which from the bathochromic shift of the ultra-violet absorption maximum and the inertness of the bromine atom must have the constitution (V). The dihydropyrone also reacted very sluggishly with *N*-bromosuccinimide, to give, after debromination, the bromo-compound (V) in poor yield.

Synthesis of 2 : 3-dihydro-3-methyl-6-phenyl-4-pyrone is under investigation.

Experimental.—Ultra-violet absorption spectra were taken in 95% EtOH.

2 : 3-*Dihydro*-3-*methyl*-6-*phenyl*-4-*pyrone* (III).—The crude solid material which separated from the steam-distillate of the essential oil was purified by crystallisation from light petroleum

(b. p. 60—80°), to give the *dihydropyrone*, m. p. 69° [Found : C, 76·7; H, 6·8; OMe, 0·0; *C*-Me, 4·7%; *M* (Rast), 170. $C_{12}H_{12}O_2$ requires C, 76·55; H, 6·4; *C*-Me, 8·0%; *M*, 188]. Ultraviolet absorption max. : 242, 295, and 303 mμ (ε 8000, 18,000, 18,000). The compound gave a yellow colour with tetranitromethane and no colour with ferric chloride. It gave a 2 : 4-*dinitrophenylhydrazone*, dark red prisms, m. p. 238°, from ethanol (Found : C, 58·6; H, 4·3; N, 14·6. $C_{18}H_{16}O_5N_4$ requires C, 59·0; H, 4·4; N. 14·8%), $\lambda_{max.}$ 412 mμ (ε 25,000).

5-Bromo-1 : 2-*dihydro*-3-*methyl*-6-*phenyl*-4-*pyrone* (V).—Bromine (220 mg., 1 mol.) in carbon tetrachloride was added slowly to the dihydropyrone (240 mg.) in carbon tetrachloride. After 10 min. the solution was concentrated to dryness *in vacuo*, then gently warmed with collidine on a water-bath for 10 min. and filtered, and the residue was kept overnight at 0° in light petroleum (b. p. 65—110°), yielding long needles of the *bromo*-compound (V) (175 mg.), m. p. 74°, unaltered by further crystallisation (Found, in a sublimed sample : C, 53·6; H, 4·1. $C_{12}H_{11}O_2Br$ requires C, 53·8; H, 4·1%), $\lambda_{max.}$ 225, 248, and 314 mμ (ε 6500, 8000, and 15,000). The bromo-compound was stable to further treatment with collidine.

Alkaline Hydrolysis of 2 : 3-*Dihydro*-3-*methyl*-6-*phenyl*-4-*pyrone*.—The dihydropyrone (190 mg.) and potassium hydroxide (200 mg.) were refluxed for 1 hr. in 50% aqueous ethanol, then steam-distilled. The distillate was passed into a solution of 2 : 4-dinitrophenylhydrazine in 1% hydrochloric acid. The precipitated 2 : 4-dinitrophenylhydrazone was filtered off and crystallised from acetic acid, to afford acetophenone 2 : 4-dinitrophenylhydrazone (30 mg.), m. p. and mixed m. p. 243° (Found : N, 18·1. Calc. for $C_{14}H_{12}O_4N_4$: N, 18·6%). No further derivatives were isolated by chromatography of the crude 2 : 4-dinitrophenylhydrazone on activated alumina.

The alkaline residue from the steam-distillation was acidified and extracted with ether, to give benzoic acid, m. p. and mixed m. p. 122°.

We are indebted to the National Research Council, Canada, for a grant and for a N.R.C. post-doctorate fellowship to one of us (B. R. T.).

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The Activation Energy of Electrical Conductivity in Fused Electrolytes.

By R. L. MARTIN.

[Reprint Order No. 5309.]

IN electrochemical investigations on molten systems, much importance is attached to the magnitude of the activation energy of ionic conduction (E_κ or E_λ) and its variation with composition, for both are closely related to the constitution of the melt and the mechanism of ionic conduction (Bloom and Heymann, *Proc. Roy. Soc.*, 1947, *A*, **188**, 392). It is generally tacitly assumed that the activation energy E_κ calculated from the equation for specific conductivity, $\kappa = \kappa_0 \exp(-E_\kappa/\boldsymbol{R}T)$, is equal to the energy of activation E_λ derived from the equation for molar conductivity, $\lambda = \lambda_0 \exp(-E_\lambda/\boldsymbol{R}T)$, but the relation between these activation energies has nowhere been explicitly examined. The present note shows that the activation energy E_λ is, in fact, necessarily greater than E_κ by an amount $\boldsymbol{R}T^2\alpha$, where α is the coefficient of thermal expansion of the melt. This result is readily derived from the following definitions of molar conductivity, coefficient of thermal expansion α, and activation energy :

$$\lambda = M\kappa\rho^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\alpha = -(1/\rho)\mathrm{d}\rho/\mathrm{d}T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$E_\kappa, E_\lambda = -\boldsymbol{R}\mathrm{d}(\ln \kappa,\lambda)/\mathrm{d}(1/T) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where M is the molecular weight and ρ the density of the melt. From equation (1),

$$\frac{d(\ln \lambda)}{d(1/T)} = \frac{d(\ln \kappa)}{d(1/T)} - \frac{d(\ln \rho)}{d(1/T)}$$

and substitution of equations (2) and (3) in this expression gives

$$E_\lambda = E_\kappa + RT^2\alpha \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

It follows from equation (4) that E_κ and E_λ can only be equated for those systems which are investigated either at relatively low temperatures (say below 400° K), or which show exceptionally small variations of density with temperature. The former class is exemplified by low-melting electrolytes such as the alkylammonium picrates and boron trifluoride co-ordination compounds (Greenwood and Martin, *J.*, 1953, 1427), and the latter includes molten silicates (Bockris, Kitchener, Ignatowicz, and Tomlinson, *Trans. Faraday Soc.*, 1952, **48**, 75). Examples of these classes of compound are given in the Table, which shows that E_λ is less than 4% greater than E_κ. However, for high-melting salts with normal values of α, such as the molten alkali halides, the term $RT^2\alpha$ becomes appreciable and E_κ and E_λ can no longer be taken as equal; *e.g.*, E_λ for sodium chloride is 80% greater than E_κ.

Values for E_κ *and* E_λ.*

Compound	M. p. (°K)	E_κ (kcal. mole^{-1})	$10^4\alpha$ (deg.$^{-1}$)	$RT^2\alpha$ (kcal. mole^{-1})	E_λ (kcal. mole^{-1})
Pr^n_4NPic †	393	7·1	7	0·2	7·3
$BF_3,2H_2O$	279	3·1	8	0·1	3·2
$Na_2O,2{\cdot}4SiO_2$	1130	10·8	1	0·2	11·0
NaCl	1074	1·5	6	1·2	2·7

* Data taken from above references and the "Handbook of Physical Constants," Geological Society of America, Special Papers No. 36, 1942.

† Tetra-*n*-propylammonium picrate.

This result bears directly on any discussion of the constitution of molten electrolytes because of the emphasis placed on the ratio $m = E_\eta/E_\kappa$, where E_η is the activation energy for viscous flow (Frenkel, "Kinetic Theory of Liquids," Clarendon Press, Oxford, 1946, Chap. VIII). Clearly, it is desirable to decide whether the ratio m or its analogue $m' = E_\eta/E_\lambda$ is the more fundamental in interpreting the mechanism of ionic conduction and viscous flow. Bloom and Heymann (*loc. cit.*) have argued in favour of E_η/E_κ rather than E_η/E_λ on the grounds that η is dimensionally more closely related to κ than to λ. However, their argument is vitiated since the dimensions of the quantities being compared (E_κ, E_λ, and E_η) are identical, being those of energy per mole. It is now suggested that λ, E_λ, and E_η/E_λ be chosen for comparison functions as this ensures that the conductivity is always related to 1 mole of electrolyte between electrodes 1 cm. apart.

The author thanks Dr. N. N. Greenwood for helpful discussions.

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Chemical Action of Ionising Radiations in Aqueous Solutions. Part XIII. Absolute Yield of the Ferrous Sulphate Dosimeter.*

By F. T. Farmer, T. Rigg, and J. Weiss.

[Reprint Order No. 5359.]

Dilute ferrous sulphate in 0·8N-sulphuric acid has, in the last few years, become a standard dosimeter for ionising radiations. Much discussion has arisen as to the absolute yield of this system, usually expressed as the G value, *i.e.*, moles of ferric salt produced per 100 ev. Miller (*J. Chem. Phys.*, 1950, **18**, 79) and Hardwick (*Canad. J. Chem.*, 1952, **30**, 17) have reported values of about $G(Fe^{III}) \simeq 20$ for gamma-rays or hard X-rays, and Rigg, Stein, and Weiss (*Proc. Roy. Soc.*, 1952, *A*, **211**, 375) reported $G = 19{\cdot}7$ for X-rays (200 kv). On the other hand, Hochanadel and Ghormley (*J. Chem. Phys.*, 1953, **21**, 880) found $G(Fe^{III}) = 15{\cdot}6$ for ^{60}Co gamma-rays, while other recent work [Lazo, Dewhurst, and Burton, 1953 Report Radiation Project, Contract AT (11—1) — 38, Univ. Notre Dame; Jerome Weiss, Bernstein, and Kuper, 1953, Brookhaven National Laboratory Report] has led to $G(Fe^{III}) = 15{\cdot}9$.

The measurements by Miller, by Hardwick, and by Jerome Weiss *et al.* (*loc. cit.*) were based on ionisation measurements in air, with the values W(air) = 32·5, 31·9, and 34·3 ev, respectively, where W(air) is the energy required to form an ion pair. Hochanadel and Ghormley's value was obtained calorimetrically, and that of Rigg *et al.* was based on the ionisation method described by Farmer, Stein, and Weiss (*J.*, 1949, 3241) who also used W(air) = 32·5 ev.

Recently, we have become aware that two corrections must be made to our previously reported value: (i) In the case of 200-kv X-rays, allowance must be made for photo-electric absorption processes in the 0·8N-sulphuric acid. (ii) Several recent investigations have shown that the W values previously used are too low; according to Valentine (*Proc. Roy. Soc.*, 1952, *A*, **211**, 75) W(air) = 35·0 ± 0·5 ev.

The former correction can be made from measurements of the apparent $G(Fe^{III})$ value at different acid concentrations. The results given in the Table show that the yield of ferric salt in 0·8N- is appreciably greater than that in 0·01N-sulphuric acid (these experiments were carried out by the method described by Rigg *et al.*, *loc. cit.*). It is clear that for the present purpose, the *initial yields* have to be considered. Thus, while it is well known that in the strongly acid solutions the yield–dose relation is linear, this is no longer true at the lower acidities, on account of the pH-dependent back-reaction, $Fe^{3+} + O_2^- \longrightarrow Fe^{2+} + O_2$, which tends to lower the yield of ferric salt (cf. Rigg *et al.*, *loc. cit.*). According to the last-named workers, there is no obvious chemical reason for an increase in the initial yield of ferric salt in the more concentrated acid solutions and it is therefore suggested that the true G value should be very close to the (initial) G value at low acidities, *e.g.*, in 0·01N-acid which is sufficiently close to pure water from the point of view of energy absorption. The increase of the yield with sulphuric acid concentration is therefore attributable to the photo-electric effect, so that the original G value is decreased from 19·7 to 18·0 (see Table).

Variation of the initial yield of ferric salt with sulphuric acid concentration for $3{\cdot}1 \times 10^{-4}$M-$FeSO_4$, *in air-saturated solution irradiated with* X-*rays* (200 kv).

Concn. of H_2SO_4 (N)	0·80	0·10	0·01
Apparent yield (Fe^{III}/100 ev), calc. with W(air) = 32·5 ev	19·7	18·2	18·0

The magnitude of the correction made here for 200-kv X-rays is also compatible with calculations based on the energy distribution in the radiation produced by the X-ray tube and with the geometry of the experimental arrangement. For 0·8N-sulphuric acid, even with X- or gamma-rays of energy greater than 1 Mev, a correction of about 2·5% must be

* Part XII, *J.*, 1954, 66.

made for the increased electron density. By using the recently established value $W(\text{air}) = 35{\cdot}0$ ev (Valentine, *loc. cit.*), the lower G value of 18·0 obtained after correction for photoelectric absorption is further lowered to $18{\cdot}0(32{\cdot}5/35{\cdot}0) = 16{\cdot}7$. Very recently, moreover, it has been discovered that a further correction must be made for geometrical factors in the standard air chamber used at the National Physical Laboratory, against which the dosimeter employed in this work was calibrated (Kemp and Hall, *Brit. J. Radiol.*, 1954, **27**, 219). This reduces the value of G by a further 3%. Taking account of the various experimental errors, which are estimated to be not more than $\pm 5\%$, we arrive, therefore, at a final value of $G(Fe^{III}) = 16{\cdot}2 \pm 0{\cdot}8$.

In the case of 200-kv X-rays, this new G value leads to the value 3·80 for the yield $G(R)$ of free radical pairs (H + OH) from water, and to 0·54 for the yield of the " molecular " decomposition $G(M)$ of water. This is based on recent measurements of Rigg and Weiss (unpublished work) which are also in agreement with the previous measurements by Allen (*Discuss. Faraday Soc.*, 1952, **12**, 79; Johnson and Allen, *J. Amer. Chem. Soc.*, 1952, **74**, 4147). Similar experiments with radium gamma-rays have shown that the ratio $G(M)/G(R)$ is about 20% less than with 200-kv X-rays; the $G(Fe^{III})$ is probably within the experimental limits given above for the X-rays, on account of the relatively small contribution of $G(M)$ to this yield.

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A Modified Synthesis of Dibenzoselenophen Oxide.

By L. CHIERICI and R. PASSERINI.

[Reprint Order No. 5254.]

DIBENZOSELENOPHEN OXIDE (I) has been prepared by treating dibenzoselenophen dibromide or dichloride with 3% aqueous sodium hydroxide (Courtot and Montamedi, *Compt. rend.*, 1934, **199**, 531; Behaghel and Hofmann, *Ber.*, 1939, **72**, 582). Recently McCullough and his associates (*J. Amer. Chem. Soc.*, 1950, **72**, 5753) described a new synthesis of dibenzoselenophen, and obtained the oxide by oxidation with 40% peracetic acid in glacial acetic acid.

Since a convenient supply of peracetic acid was not readily available, and every attempted oxidation with hydrogen peroxide in glacial acetic acid failed, we modified the methods already reported. As stated by McCullough and his co-workers the direct bromination of bis-2-diphenylyl diselenide by Behaghel and Hofmann's method leads to a mixture of dibenzoselenophen dibromide and bromodibenzoselenophen dibromide. We found that addition of bromine to a chloroform solution of 2-selenocyanatodiphenyl gives a good yield of dibenzoselenophen dibromide. From the latter, dibenzoselenophen oxide can be easily obtained as indicated by Courtot and Montamedi (*loc. cit.*).

(II) (III) (IV) (I)

The present synthesis is more convenient than those already recorded, and appears to be particularly suitable for the preparation of dibenzoselenophen oxide from 2-aminodiphenyl.

Experimental.—*2-Selenocyanatodiphenyl* (III). 2-Aminodiphenyl (80 g.) was diazotised in dilute hydrochloric acid, and cold aqueous potassium selenocyanate (80 g.) added to the neutralised (Congo red) solution. Vigorous stirring was continued for 1 hr., then the mixture was

allowed to decompose for 6 hr. The reddish oil was extracted with ether, the ether extract dried (Na_2SO_4), the excess of ether removed, and the oil distilled at reduced pressure. An orange-coloured product (70 g.), b. p. 193—195/10 mm., was obtained.

Dibenzoselenophen dibromide (IV). To a solution of 2-selenocyanatodiphenyl (51 g.) in chloroform (275 c.c.), bromine (20 c.c.) was added dropwise during 3 hr., and external cooling (running water) was then continued for another 3 hr. The mixture was then set aside at room temperature for 12 hr. and finally heated at 70° for 24 hr. Evolution of hydrogen bromide having then ceased the mixture was filtered and the precipitate washed with little chloroform. Dibenzoselenophen dibromide formed red needles (80%), m. p. 122° (Found : Se, 20·35. Calc. for $C_{12}H_8SeBr_2$: Se, 20·2%).

Dibenzoselenophen oxide (I). A suspension of the dibromide (20 g.) in aqueous sodium hydroxide (3% ; 150 c.c.) was then thoroughly stirred at room temperature. The red solution became practically colourless during 1½ hr. and was then heated on a water-bath for 2—3 min. The cooled suspension was filtered and the precipitate crystallized from aqueous ethanol; it had m. p. 207—208° (Found : Se, 32·05. Calc. for $C_{12}H_8OSe$: Se, 32·0%).

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Raman Effect and Suggested Complexity of the Argentous Ion in Solution.

By D. N. WATERS and L. A. WOODWARD.

[Reprint Order No. 5404.]

RECENT investigations of aqueous solutions of silver salts (Davies and Morgan, *Chem. and Ind.*, 1954, 428) have shown anomalies, which can be accounted for by the hypothesis (Davies and Morgan, *loc. cit.*) that in solution the argentous ion exists to a considerable extent as Ag_2^{++}.

It is therefore of interest to test this hypothesis by an independent and more direct method. The Raman effect offers such a possibility; for if monatomic, the ion will show no vibrational frequency, whereas if it is diatomic, a single frequency should be observed. The method has been applied successfully (Woodward, *Phil. Mag.*, 1934, **18**, 823) to show that the mercurous ion exists in solution as Hg_2^{++}. The force constant of the hypothetical Ag_2^{++} being assumed to be about the same as that of Hg_2^{++}, the Raman frequency of the former should be about $\Delta\nu = 230$ cm.$^{-1}$, which is more favourable for observation than that of the mercurous ion.

Experimental.—A concentrated aqueous solution of silver nitrate (8·4 g.-atoms of silver per l.) was investigated, the Raman apparatus previously described being used (George, Rolfe, and Woodward, *Trans. Faraday Soc.*, 1953, **49**, 375). Excellent spectra were obtained with exposure times up to 2 hr. These showed the complete Raman effect of the nitrate ion, but no trace of a line attributable to Ag_2^{++}.

To set against this negative result the mercurous ion was re-investigated. With a mercurous nitrate solution containing only 0·62 g.-atom of mercury per l. and the same technique as for silver nitrate the Raman frequency of Hg_2^{++} was obtained with an exposure time of only 2 min.

Discussion.—In the association of ions of opposite sign, failure to observe a characteristic Raman effect may be accounted for (George, Rolfe, and Woodward, *loc. cit.*) by supposing that the ions are held together by electrostatic forces, no chemical linkage being involved; but for the association of two ions of the same sign (as in Ag_2^{++}) the absence of a Raman line cannot be so explained.

If we assume that the intrinsic Raman intensity of the hypothetical Ag_2^{++} is the same as that of Hg_2^{++}, it follows at once from the concentrations and exposure times given above that not more than 0·1% of the total silver could have been present in the form of Ag_2^{++}.

Since the atomic number of silver is roughly half that of mercury, there are some grounds for believing (cf. Woodward and Long, *Trans. Faraday Soc.*, 1949, **45**, 1131) that on this account the Raman intensity of Ag_2^{++} would be somewhat lower (perhaps by a factor of about 4) than that of Hg_2^{++}. Even so it is improbable that as much as 1% of the silver could have been present in the form of double ions, despite the high concentration of the solution investigated.

If, on the contrary, we assume that a high proportion of the silver was indeed present as Ag_2^{++}, then it follows conversely that the intrinsic Raman intensity of this species must be at least 1000 times smaller than that of Hg_2^{++}. It is true that the type of covalent bonding in Ag_2^{++} cannot be the same as in Hg_2^{++}; for whereas Hg^+ possesses a single *s*-electron, the pairing of which with a similar *s*-electron belonging to a second Hg^+ doubtless gives rise to the bond in ($Hg–Hg^{++}$), the Ag^+ ion possesses no such *s*-electron. The nature of the covalent bond in the hypothetical Ag_2^{++} is not clear, and it is possible that the species might have an unusually low Raman intensity; but a value 1000 or more times less than for Hg_2^{++} appears improbable. The non-appearance of a Raman effect therefore throws considerable doubt on the hypothesis of the existence of the double argentous ion in appreciable concentration.

We are grateful to Mr. R. P. Bell for having suggested these experiments and to Prof. C. W. Davies for his interest and for permission to refer to his forthcoming paper.

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Complex Fluorides. Part III. Lattice Constants of Some Complex Fluorides of Lithium or Sodium and Quadrivalent Elements.*

By B. Cox.

[Reprint Order No. 5331.]

WHEREAS many partial and several complete structure determinations have been made on complex fluorides of formula A_2MF_6, where A = K, Rb, Cs, NH_2, or Tl, no information is available at present on analogous lithium and sodium salts. In the course of investigations on complexes of quadrivalent elements, it has been found by *X*-ray powder photography that sodium fluorosilicate, fluorotitanate, fluorogermanate, fluoromanganate, and fluoroplatinate form an isomorphous series. Lattice constants for the hexagonal unit cells are: Na_2SiF_6, $a = 8{\cdot}86$, $c = 5{\cdot}02$; Na_2TiF_6, $a = 9{\cdot}21$, $c = 5{\cdot}15$; Na_2GeF_6, $a = 9{\cdot}10$, $c = 5{\cdot}13$; Na_2MnF_6, $a = 9{\cdot}03$, $c = 5{\cdot}13$; Na_2PtF_6, $a = 9{\cdot}41$, $c = 5{\cdot}16$ Å. Lithium fluorosilicate is isomorphous with the sodium salts, with $a = 8{\cdot}22$, $c = 4{\cdot}56$ Å; lithium fluorogermanate gives a powder pattern which, though similar in appearance to that of the fluorosilicate, cannot be indexed completely on the basis of a hexagonal unit cell; and the same applies, though to a greater degree, to lithium fluorotitanate. It is hoped to publish later a full determination of the structure of sodium fluorosilicate.

Experimental.—Sodium hexafluoromanganate(IV) was prepared by electrolytic oxidation of manganous fluoride and sodium fluoride in 40% hydrofluoric acid, as described in Part II for the ammonium salt. The solubility of the sodium salt in 40% hydrofluoric acid precluded the use of the acid for washing out any sodium fluoride present (Found: Mn, 23·3. Na_2MnF_6 requires Mn, 25·6%).

The *fluoroplatinate* was obtained by fluorination of sodium chloroplatinate with bromine trifluoride (see Sharpe, *J.*, 1950, 3444, for a description of the method); the product of the reaction was heated at 200° for 30 min., dissolved in cold water, and precipitated by addition of alcohol (Found: Pt, 54·1. Na_2PtF_6 requires Pt, 54·9%). Sodium fluorotitanate (Hunter, *J. Amer. Chem. Soc.*, 1910, **32**, 330) and fluorogermanate (Muller, *Proc. Amer. Phil. Soc.*, Suppl.

* Part II, *J.*, 1954, 1798.

5, 1926, **65**, 44; *Chem. Abs.*, 1927, **21**, 3171) were prepared from the dioxides, hydrofluoric acid, and sodium fluoride (Found, for the fluorotitanate: Ti, 23·0; Calc. for Na_2TiF_6: Ti, 23·1. Found, for the fluorogermanate: Ge, 29·8; Na, 20·3; Calc. for Na_2GeF_6: Ge, 31·2; Na, 19·8%). The sodium fluorosilicate used was a pure commercial product. Lithium salts were prepared from the dioxides, hydrofluoric acid, and lithium carbonate (Found, for the fluorosilicate: Li, 8·9. Calc. for Li_2SiF_6: Li, 8·9. Found, for the fluorogermanate: Li, 6·9. Calc. for Li_2GeF_6: Li, 6·9. Found, for the fluorotitanate: Ti, 27·6. Calc. for Li_2TiF_6: Ti, 27·2%).

X-Ray powder photographs were taken and interpreted as described in Part II. The calculated density of sodium fluorosilicate, on the assumption of 3 mols. per unit cell, is 2·73; this compares with a value of 2·75 found by Stolba (*Z. anal. Chem.*, 1872, **11**, 199).

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University Chemical Laboratory, Cambridge. [*Received, April 26th*, 1954.]

8-*Amino*-6-*methoxyquinoline, and Some Derivatives of* 5 : 5′-*Diquinolyl.*

By W. V. Farrar.

[Reprint Order No. 5337.]

8-Amino-6-methoxyquinoline is reported to melt at 40—41° (*inter al.*, B.P. 267,169; Altman, *Rec. Trav. chim.*, 1938, **57**, 941; Crum and Robinson, *J.*, 1943, 561). Chichibabin and Hoffmann, however (*Compt. rend.*, 1939, **208**, 535), report m. p. 52°, alleging that the lower-melting products were contaminated with 6-methoxyquinoline. The amine is in fact dimorphic.

In the reduction of 6-methoxy-8-nitroquinoline with iron and ferrous chloride in ethanol, considerable quantities of a high-melting crystalline by-product were observed which was shown to be 8 : 8′-diamino-6 : 6′-dimethoxy-5 : 5′-diquinolyl. Its formation is probably due to the oxidation of the aminoquinoline by ferric salts, a reaction which was found to give the diquinolyl derivative in 45—50% yield. A similar oxidation of α-naphthylamine gives naphthidine (Reverdin and de la Harpe, *Chem. Ztg.*, 1892, **16**, 1687; Sah and Yuin, *Rec. Trav. chim.*, 1939, **58**, 751), but the reaction is not very general. 5- and 6-Aminoquinolines do not react; 8-amino-6-hydroxyquinoline, 1-aminoacridine, and 8-nitro-1-naphthylamine gave complex and unidentifiable products. From 8-aminoquinoline, however, 8 : 8′-diamino-5 : 5′-diquinolyl was obtained in *ca.* 5% yield. The structure of this substance was confirmed by hydrolysis with hydrochloric acid, which gave a small yield of the known 8 : 8′-dihydroxy-5 : 5′-diquinolyl (Bratz and Niementowski, *Ber.*, 1919, **52**, 189). The 5 : 5′-orientation of this compound is known from its synthesis by an unambiguous Skraup reaction.

Experimental.—8 : 8′-*Diamino*-6 : 6′-*dimethoxy*-5 : 5′-*diquinolyl.* (*a*) Iron borings (260 g.), ethanol (500 g.), water (150 g.), and ferrous chloride (10 g.) were stirred together at 65° in an iron vessel fitted with a glass reflux condenser. 6-Methoxy-8-nitroquinoline (95% pure, 215 g.) was added during 1·5 hr. without external heating. During the addition, hydrochloric acid (10 c.c.) had to be added to keep iron in solution (sodium sulphide test). The mixture, after refluxing for 2 hr., was basified with sodium carbonate and filtered, and the filter-cake was washed with hot ethanol. The filtrate and washings were freed from solvent and finally distilled *in vacuo*, giving 8-amino-6-methoxyquinoline, b. p. 169—171°/3 mm. (104 g.). The first two of a series of preparations gave distilled material, m. p. 38—40°; the molten product was poured into glass bottles and allowed to solidify. After three weeks, both bottles had cracked, owing to expansion of their contents, which now had m. p. 49—51°. All subsequent preparations had this higher m. p.

The non-volatile residue was broken up and extracted with acetone; the extracts, on standing, gave brownish crystals (26 g.) of crude diquinolyl compound.

(*b*) 8-Amino-6-methoxyquinoline (5 g.), hydrated ferric chloride (15 g.), hydrochloric acid (10 c.c.), and water (100 c.c.) were refluxed for 1 hr., basified with aqueous sodium hydroxide, and filtered, and the solid product was washed and dried. Extraction with acetone (Soxhlet) gave the almost pure diquinolyl derivative (2·25 g., 45%).

Recrystallisation of diquinolyl products from (*a*) or (*b*) from acetone gave large yellow-brown prisms of a *solvate*, which lost acetone at 60° (loss, 24·7. $C_{20}H_{18}O_2N_2,2C_3H_6O$ requires loss 25·1%); the material became opaque and sulphur-yellow and then had m. p. 252° (decomp.) [Found: C, 69·6; H, 5·2; N, 16·3; OMe, 16·8%; *M* (Rast), 326, (nitrite titration, $2NH_2$-groups) 348. $C_{20}H_{18}O_2N_4$ requires C, 69·4; H, 5·2; N, 16·2; OMe, 17·9%; *M*, 346]. The compound is sparingly soluble in the common solvents; like other derivatives of 8-aminoquinoline, it forms orange salts. The *diacetyl* derivative formed colourless needles, m. p. 289—290°, from acetone (Found: C, 66·55; H, 5·35. $C_{24}H_{22}O_4N_4$ requires C, 66·9; H, 5·15%).

8 : 8′-*Diamino*-5 : 5′-*diquinolyl* was made from 8-aminoquinoline by method (*b*) in *ca.* 5% yield. It formed yellow crystals, m. p. 262° (decomp.) from acetone, or platelets from dioxan (Found: C, 75·3; H, 4·55; N, 19·35. $C_{18}H_{14}N_4$ requires C, 75·5; H, 4·9; N, 19·6%). The *diacetyl* derivative, pale yellow platelets from *n*-butanol, had m. p. 318—320° (decomp.) (Found: N, 14·7. $C_{22}H_{18}O_2N_4$ requires N, 15·1%).

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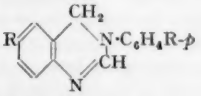
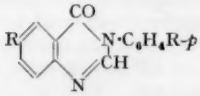
The Oxidation of Some Quinazoline Derivatives.

By W. V. FARRAR.

[Reprint Order No. 5338.]

THE reaction of *p*-fluoroaniline with formaldehyde in acid solution gives a substance $C_{14}H_{10}N_2F_2$, which by analogy with similar products from *p*-chloro- and *p*-bromo-aniline (Wagner and Eisner, *J. Amer. Chem. Soc.*, 1937, **59**, 479) is probably (I; R = F). The most remarkable property of this compound is its ready oxidation at its melting point to the quinazolone (II; R = F), more conveniently obtained from it by use of permanganate.

(I)  (II) 

The corresponding chlorine compound (I; R = Cl) is similarly oxidised at its melting point, but not so rapidly. The bromine compound (II; R = Br) was found by Cairncross and Bogert (*Coll. Czech. Chem. Comm.*, 1935, **7**, 548) among the products of the reaction between *p*-bromoaniline and formaldehyde; it was not found by Wagner and Eisner (*loc. cit.*); it almost certainly arose by aerial oxidation of (I; R = Br) during the lengthy manipulations carried out by the former workers.

Experimental.—6-*Fluoro*-3-p-*fluorophenyl*-3 : 4-*dihydroquinazoline* (I; R = F). *p*-Fluoroaniline hydrochloride (5·5 g.) was dissolved in hydrochloric acid (5 c.c.) and water (45 c.c.), and 37% formaldehyde solution (10 c.c.) was added. After 4 days, the insoluble hydrochloride was collected, taken up in hot water, filtered, and basified. Recrystallisation from aqueous ethanol gave needles (1·65 g.), m. p. 137—138° with resolidification (Found: C, 68·5; H, 4·2; N, 11·0. $C_{14}H_{10}N_2F_2$ requires C, 68·85; H, 4·1; N, 11·45%).

6-*Fluoro*-3-p-*fluorophenylquinazol*-4-*one* (II; R = F). (*a*) The quinazoline (0·5 g.) was fused for 2 min. Extraction with ethanol gave two products in approximately equal amounts, the soluble one being unchanged starting material. The other, very sparingly soluble, was the

quinazolone, forming hair-like needles, m. p. 260°, from much ethanol (Found: C, 64·8; H, 3·5; H, 10·7. $C_{14}H_8ON_2F_2$ requires C, 65·1; H, 3·15; N, 10·85%).

(*b*) The quinazoline (0·6 g.) in acetone (50 c.c.) was treated with powdered potassium permanganate until the solution was permanently pink, then added to excess of sodium hydrogen sulphite solution. The precipitated quinazolone was recrystallised from much ethanol (0·43 g., 70% yield).

The chlorine *analogue* (II; R = Cl), made by method (*b*) in 85% yield, formed fine needles (from much ethanol), m. p. 225° (Found: C, 57·7; H, 2·9; Cl, 24·4. $C_{14}H_8ON_2Cl_2$ requires C, 57·7; H, 2·75; Cl, 24·4%). This substance may be identical with an unanalysed compound, m. p. 225°, prepared by Bischoff and Reinfeld (*Ber.*, 1903, **36**, 41), but this part of these authors' work could not be repeated.

IMPERIAL CHEMICAL INDUSTRIES LIMITED, DYESTUFFS DIVISION,
HEXAGON HOUSE, BLACKLEY, MANCHESTER, 9. [*Received, April 28th*, 1954.]

OBITUARY NOTICE.

EDWARD MORTIMER CROWTHER.

1897—1954.

AGRICULTURAL chemists in many countries will learn with regret that Edward Mortimer Crowther of the Rothamsted Experiment Station died of heart trouble on March 17th, 1954, at the Dunstable Hospital, Luton, after a very brief illness. He was born at Horsforth near Leeds on April 15th, 1897. Starting at an elementary school he gained scholarships first to Archbishop Holgate's School, York, and then in 1914 to Leeds University where in 1917 he took an Honours degree in Chemistry. Strongly objecting to military service he was assigned to the Rothamsted Experimental Station, then engaged on the difficult task of helping to produce more food in Great Britain under the severe handicap of heavily curtailed supplies of skilled labour and of fertilizers. Munition makers had the first claim on ammonia, nitrates, and the sulphuric acid needed for making superphosphate; there was as yet no synthetic nitrogen industry in this country; the only source of ammonia was from coal; nitrate and sulphur both had to be imported at heavy risk of loss by submarines. Food supplies from overseas were being sunk daily and the position was serious.

At Rothamsted Crowther was attached to a small group searching for fertilizer materials among the waste products of industry and of the cities. He proved so able and trustworthy that at the end of the war he was appointed permanently to the staff.

The war had shown how greatly science could help agriculture and after it was over Rothamsted received substantial grants for expansion. It was, however, necessary to make fundamental changes in agricultural science itself. Hitherto it had been regarded as a branch of chemistry; as it developed it had to be linked with the physical and biological sciences. An ill-defined hybrid subject, descriptive only, might have resulted, but the policy adopted at Rothamsted was to put it on a firm quantitative basis, aiming at as high standards of accuracy as possible. A statistical section was set up under R. A. Fisher and principles of experimentation were worked out which allowed the probable error of each experiment to be calculated and also enabled plans of experiments to be devised in which the error should be within a specified limit. The men and women selected to work on these lines had to be, not only well trained in their science, but also sufficiently receptive mentally to be able to assimilate the new principles and to base their investigations on them. Crowther satisfied these conditions extraordinarily well.

He was put into the new Physics Department under B. A. Keen and began by studying the methods of determining soil acidity, a condition then attracting much attention because of the losses of crop resulting therefrom. Various titration methods had been devised for its estimation, but doubts were arising whether any of them was adequate: Crowther confirmed the view that the hydrogen-ion concentration must be determined and he devised a practicable method bywhich this might be done simply and with sufficient accuracy. Recognising the value of one of the titration methods for a busy analyst he showed how it might be used to the greatest advantage, and with what limitations. This work led to a study of the various liming materials.

He also studied some of the colloidal properties of soils. It was then generally assumed that the particles of the soil were coated with a colloidal gel which gave it some of its special properties: he showed however that some of the phenomena could be explained by postulating a system of micropores or capillaries in the soil, and also that the colloidal portion had a reticulate structure possibly analogous to that of silica gel.

In 1923 the Empire Cotton Corporation established a soil research post at Rothamsted and Crowther was the obvious man to fill it; later he spent six months (1925—26) at Wad Medani in the Sudan to study the difficult problems arising out of the irrigation of the very heavy Gezira soil on which the valuable long-stapled cotton was grown. He retained his association with this great project all his life.

He was probably best known for his studies of the chemical aspects of soil fertility, and in particular for his attempts to estimate the fertilizer requirements of crops by chemical analysis of the soil. The last problem was an old one, but little progress had been made with it because of the dearth of precise field experiments for the standardisation of the methods. When Fisher's new principles were enunciated Crowther realised that they could furnish data of the kind needed; along with T. Eden and H. V. Garner he put into practical shape these new

statistical principles and made them an integral part of agricultural experimentation. It was a great satisfaction to him (as indeed to all the Rothamsted workers) to hear the distinguished physicist, Sir Harold Jeffries, declare at the British Association meeting of 1953 that, thanks to these new methods, " the standard of presentation of results in agriculture is better than in any of the so-called exact sciences; " adding also " this is a state of affairs that physicists should cease to tolerate."

When the Government decided to encourage the growth of sugar beet in this country Rothamsted was asked to carry out extensive fertilizer trials. These were started in 1926 under Crowther's direction, in co-operation with the factory organisation, and they were planned on the new lines so as to give the growers the information they needed, and at the same time provide the chemist with the standardised plots of soil he had long wanted. The experiments are still continuing; unfortunately Crowther did not complete the examination of the results, but the data are fully recorded. Other crops came under experiment, not on the same scale but equally well-designed; the plan also included where necessary systematic chemical studies of the produce and of the soil. He was never satisfied with what he called the crude yields.

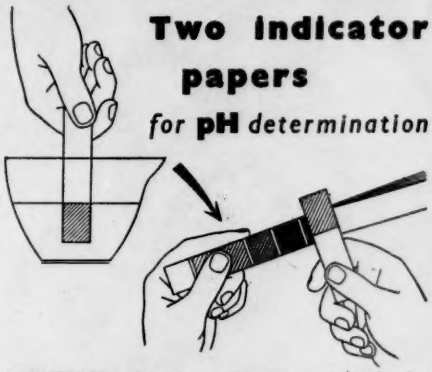
Nor was his work confined to this country. In conjunction with W. B. Haines, then of the Dunlop Estates, Malaya, he organised a remarkably well-planned and extensive series of fertilizer experiments on rubber trees; and, as the result of a visit to West Africa, another set on the effects of fertilizers on the oil palm. In both instances these are by far the best experiments yet made. In recent years he had made some promising investigations of the problems of forestry plantations in this country.

He did a considerable amount of work also on phosphatic fertilizers, especially basic slag and water-insoluble calcium phosphates; this was in anticipation of the shortage of sulphur which has at times threatened to limit the supplies of superphosphate and may still be a cause of serious trouble. In view of the shortage of organic manures he made extensive studies of the fertilizer value of sewage sludges, straw, and other organic waste materials. He also initiated experiments in conjunction with G. W. Cooke on the proper placement of fertilizers in the soil to ensure their optimum effectiveness. His wide knowledge of the action of fertilizers proved of great service during the last war, and proposals for their effective use made by him and Dr. F. Yates were adopted as the basis of the fertilizer rationing scheme.

His keen searching criticism of the results obtained in his Department often delayed their full publication pending further examination of some points that had arisen and that he thought might vitiate them; this could not always be done at the time, so that much of his work remained incomplete and the accounts still rest in his files. It was a disappointment to his friends that the important investigations he started on the effect of climate on soil formation were never completed : the first paper published by the Royal Society in 1930 had shown a promising new approach and he always spoke with interest of the later studies he had made but not yet written up.

It is difficult to speak too highly of him as a colleague. He had the high moral character, the trustworthiness and integrity, that one expects from a member of the Society of Friends. Rothamsted passed through some anxious times during his years of service there, but his colleagues always knew that whatever might come they could rely implicitly on his loyalty and his unswerving faithfulness in following the course that he believed to be right.

E. JOHN RUSSELL.



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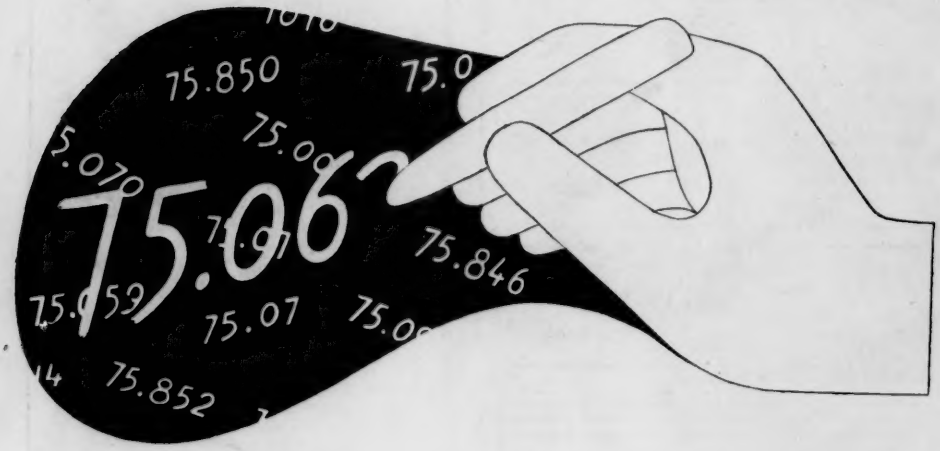

DR. MARCHAND OF BERLIN made this statement in a letter recorded in the first volume of the Proceedings of the Chemical Society (1841), challenging the claim of Liebig and Redtenbacher to have established 75.854 as the correct atomic weight for carbon. In those days atomic weights were related to oxygen as 100, and it is notable that the 1951 atomic weight for carbon calculated on this basis is 75.063 compared with Marchand's figure of 75.07 derived from the combustion of diamond and graphite.

Dr. Marchand, whose methods were simple and direct, would have welcomed the convenience and accuracy of 'AnalaR' reagents. It is even possible that they would have assisted the highly elaborate analytical work of Liebig and Redtenbacher to a more successful result.

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